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DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED AGENCIES APPROPRIATIONS FOR 1991

HEARINGS

BEFORE A

SUBCOMMITTEE OF THE

COMMITTEE ON APPROPRIATIONS

HOUSE OF REPRESENTATIVES

ONE HUNDRED FIRST CONGRESS

SECOND SESSION

SUBCOMMITTEE ON THE DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED AGENCIES

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DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, EDUCATION, AND RELATED AGENCIES FOR APPROPRIATIONS FOR 1991

THURSDAY, FEBRUARY 8, 1990.

OFFICE OF THE SECRETARY OF HEALTH AND HUMAN SERVICES

WITNESS

LOUIS W. SULLIVAN, SECRETARY

CHAIRMAN'S OPENING STATEMENT

Mr. NATCHER. The committee will come to order.

Mr. Secretary, it's an honor to have you appear before our committee. And in the beginning, I want you to know that as one Member of the committee, I think that you are making an excellent Secretary.

Secretary SULLIVAN. Thank you.

Mr. NATCHER. As you know, the 1991 budget in your department is $464 billion in outlays and almost $600 billion in budget authority.

This is larger than the budgets of all but a few countries around the world.

You have a massive and difficult job as Secretary, whether it's providing services to Social Security recipients, controlling health care costs under Medicare, or managing research of the National Institutes of Health.

From time to time, Mr. Secretary, I have people ask me how many presidents I have served with. I have served with eight presidents, and I always thought that President Eisenhower was an outstanding president because he was the one who set up the Department of Health and Human Services, brought about the interstate highway system, and had nerve enough, Mr. Secretary, to ask that the Internal Revenue Code be revised. You know they all talk around that one, but not the President.

Also, Mr. Secretary, I want to thank you and your staff on behalf of the subcommittee for their help to our staff in preparing the budget materials that we are using. They have been of great help to us, and I want you to know that we appreciate it.

And before taking your statement, Mr. Secretary, I want to present to you the chairman of the full Committee on Appropriations, Mr. Whitten of Mississippi.

Mr. Whitten of Mississippi got here, Mr. Secretary, right after World War I or World War II, I forget even just exactly which one it was. But I want to present him to you, and we are glad to have you, if you want to just say a word.

Mr. WHITTEN. Thank you very much, Mr. Chairman.

I came here to stay three years, but I can't finish the job. I agree with everything that the chairman said. I would note that in Appropriations, Mr. Natcher does a good job. Sometimes it is difficult for me to attend all of the Subcommittees but I attend when I can.

I have three meetings this morning at the same time. But it is a pleasure to be here, and Mr. Secretary, I agree with the words said by the chairman. This, I think, is the subcommittee that comes nearest to reaching all the people in the United States.

You cannot touch people any better than the subjects that are before this committee. And I am proud of every step that they made, and I have been on their side all along.

I am proud to be a Member of this subcommittee this morning, and again, it's a pleasure to work with you, and we think you are doing a great job.

Thank you, Mr. Chairman. I appreciate it.

Mr. NATCHER. Thank you, Mr. Chairman, and further, Mr. Secretary, before receiving your statement, I want to yield at this time to my friend, Silvio Conte, from Massachusetts. We work together with the other Members of this subcommittee and try to work out a good bill. When we take it over to the House floor, they stay with us, Mr. Secretary, and you know we need help every day on this committee.

My friend Silvio Conte and I along with the other Members of this subcommittee work hard on this bill, and if the House stays with us, we are going to pass you a good bill this time, Mr. Secretary.

Mr. Conte, I yield to you.

Mr. CONTE. Thank you, Mr. Chairman. Dr. Sullivan, it's truly a pleasure to have you before our committee to testify again. I offer you my warm and heartfelt greetings, as an old friend and colleague, and send my best wishes to your lovely wife, who is from my district in Pittsfield.

Doctor, I must say you have done a tremendous job in your rookie season in Washington. And you deserve special congratulations for stopping that Uptown cigarette, which was cynically marketed toward minorities.

As a former manager of the Republican baseball team, I keep a very sharp eye on talent, and I am happy to say that you have made the first team.

Secretary SULLIVAN. Thank you.

Mr. CONTE. I am also pleased to see that you are settling a real top-notch team at HHS. You have got an all star line-up, along with your veterans, Dr. Mason and Dr. Goodwin and Dick Kusserow.

You have got Antonia Novello, who soon will be the Surgeon General, and Gwendolyn King over there at Social Security, and Gail Willensky at HCFA, and Dr. Roper, CDC, Jerry Clinton at the new Agency for Health Policy and Research, Dr. Bill Harmon at HRSA, and several others.

That is a great squad, and I am sure that you all can make the Hall of Fame today.

We have got so many doctors over there that I had to hire one myself just to keep up with you, and I am looking forward to working with you this year, and I have got a lot of questions when it comes around to the time for questioning.

And I will just say it's a pleasure to work with you.

Thank you, Mr. Chairman.

Mr. NATCHER. Thank you, Mr. Conte.

Mr. Secretary, I will yield later to these other Members of the subcommittee, but at this time, we would be pleased to hear from you.

SECRETARY'S OPENING REMARKS

Secretary SULLIVAN. Thank you very much, Mr. Chairman. It's certainly a great pleasure to have this opportunity to appear before you for the second time as Secretary of Health and Human Services, though as you know in my former career, I appeared before this committee concerning support for programs in medical education. I always have been pleased and gratified with the warm reception that I have gotten from you and the other members of the committee. It's a great pleasure to be here with you.

Our appropriation request for this year, as you noted, totals $464 billion, 38 percent of Federal expenditures, and this committee is concerned with $136.8 billion of the total budget authority.

This $136.8 billion represents a $12.4 billion increase over fiscal year 1990, an increase of almost 10 percent.

Our budget reflects the President's and my own priorities for the Department. As you and I are aware, several of our goals in 1990 were not fully achieved, a prime example being the expansion of Head Start.

This year, we are seeking an unprecedented increase of $500 million for the program, which will open new doors of opportunity for an additional 180,000 children and their parents.

I want you to know that I share the President's enthusiasm for this program. In the spirit of cooperation, we must work together to get every dollar of this requested increase.

But we were also disappointed last year that funds we received for the homeless, for the Human Genome Project, and for AIDS were less than we requested.

In each of these areas, I am back this year asking for more, and I hope that together we can work to bring about these requested increases.

For fiscal year 1991, the Department's efforts to improve the health and the well-being of the American people will emphasize my major goals which are: Helping children, strengthening families, investing in the future through biomedical research, improving access to health care, promoting good health, fighting AIDS, combatting drug abuse, and prudently managing our large entitlement programs, as well as increasing the quality of the services we provide to our citizens.

Let me comment in some detail about our request. For Head Start, we are asking for a 36 percent increase, bringing the total

for Head Start to $1.9 billion. The expansion of Head Start is a key ingredient in assuring that all of our children start school ready to learn, one of our national education goals.

The addition of $500 million will allow 180,000 additional children to receive the learning skills and confidence that Head Start offers. I hope that the Congress shares this goal and will support this critical increase. Every eligible disadvantaged four year old deserves the opportunity to enjoy a Head Start experience.

As part of our expanded support for families in need, we are requesting the full authorized ceiling of $1 billion for the new Job Opportunities and Basic Skills (JOBS) training program.

The education, training and work activities provided by the JOBS program are essential for restoring dignity to families on Aid to Families with Dependent Children (AFDC) and readying them for the employment opportunities this decade will bring.

Our request will enable the 23 states without JOBS programs to implement them, as is required by law, by October 1st of this year. To provide additional assistance for parents entering the work place, support for JOBS will increase by $283 million to a total of $489 million.

Increased availability of child care services will allow more AFDC parents the opportunity to complete education, training and work programs and move themselves and their families permanently off welfare and out of poverty.

To bring about much needed reforms in the areas of child welfare and foster care, we are requesting a $47 million increase for child welfare services. This increase of 19 percent will help communities manage increasing and more difficult case loads.

Additionally, we are proposing a 10 percent limitation on annual increases in foster care administrative costs. This limitation will keep these costs in check, but will not interfere with payments to foster families or training of parents and staff.

Again, this year, the President and I are making good our promise to help America's homeless. We are requesting $233 million, $27 million of which was provided in 1990.

Last year, the Congress did not meet our request of $270 million in this area. This year, we hope that Health and Human Services health care and community service programs targeted at our homeless population will be funded at the levels of our request.

On January 24th, in announcing his new national drug control strategy, the President renewed his commitment toward demand reduction efforts. To address this and other HHS anti-drug abuse activities, we have included $1.7 billion in our request.

This level of funding will allow increases in almost all aspects of this Department's efforts to win the war on drugs. It will also provide for new initiatives, including a $50 million community prevention grant program, and a $6 million project providing nonmedical services for infants born addicted to Crack.

The American public is demanding much more action in preventing and treating drug abuse, and we are responding to this call for help.

As part of this budget, our efforts for increasing access to quality health care will focus on disadvantaged, pregnant women and their

infants. Clearly, the fact that the United States ranks eighteenth among the industrialized nations in infant mortality is disgraceful.

To concentrate on improvement in this area, our budget includes an increase of $63 million for Public Health Service programs aimed at reducing adverse pregnancy outcomes and improving infant survival.

It also fully funds the enacted Medicaid expansion for pregnant women and their children with incomes at or below 133 percent of poverty.

Death rates for minorities for heart disease, cancer, stroke, AIDS, and other disorders are far greater than those of the population as a whole. So correcting the disparity in health status between minority and nonminority populations remains one of my highest priorities.

To this end, we are seeking $117 million for a new initiative to improve access to health care for low-income minorities. This will include increasing the number of minority health professionals and initiating innovative community based approaches to recruiting minorities into health careers.

We will also develop new strategies for delivering needed health services to our minority populations. In addition, our budget includes $357 million for access to care for rural Americans. Ninety-two percent of this amount, or $327 million, will be spent on services for rural communities. This includes continuation of those activities initiated by the Congress last year for disease prevention and information outreach.

Thirty million dollars is earmarked for research on the special conditions impeding access to quality care in rural settings. We also plan to spend $9.4 million to support alcohol, drug abuse, and mental health Administration research projects and services which specifically focus on mental health services in rural areas.

The future challenges of this decade demand continued advancement of our Nation's research enterprise. In fiscal year 1991, we will provide a total of $8.9 billion for biomedical and behaviorial research. Our $436 million increase will strengthen the basic research and development efforts of the National Institutes of Health and the Alcohol, Drug Abuse and Mental Health Administration [ADAMHA].

Included in this increase is a major expansion for the Human Genome Project. This research is expected to have a profound effect on our ability to treat the more than 3,500 diseases of known genetic origin.

The project was recently named by researchers in a national survey as the number one Federally funded major science initiative, surpassing even the super-collider in the survey.

This must remain one of our highest priorities. We are planning an increase of $46 million over the $60 million Congress provided in 1990.

To begin the much needed infrastructure repair on the NIH campus, I am requesting $89 million. We can no longer continue to ignore the fundamental needs of our researchers. Facilities must be well maintained and needed renovations must occur.

Coming to AIDS, we must work until our efforts match the threat of this disease to our society. In 1991, we propose to spend

$3.1 billion on AIDS. We are requesting $1.7 billion for HIV and AIDS related activities of the Public Health Service. This increase of $109 million for the Public Health Service's efforts on AIDS will be used for continued research, for education, epidemiology, and the investigation of new drugs.

In addition, there is a $780 million increase for Medicare and Medicaid services for AIDS and HIV infected individuals. One hundred ten million dollars is also included for the newly established Agency for Health Care Policy and Research.

This amount includes funds for an expanded medical treatment effectiveness program. The effectiveness program is a comprehensive effort to learn which medical procedures are most effective for treating specific health conditions. Effectiveness research is a long-term commitment toward improving the quality of medical care, as well as reducing unnecessary medical treatments.

I am committed to ensuring the quality of service provided to the public through the large entitlement programs administered by this Department; Social Security, Medicare, and Medicaid. In 1991, we are requesting increases for the Social Security Administration and the Health Care Financing Administration, which will enable us to continue to manage these programs efficiently and effectively.

The budget included full funding for Social Security, for Supplemental Security Income, and Black Lung benefits. In addition, we are requesting $4.2 billion, an increase of $330 million, for the Social Security Administration to run these programs.

These funds will allow the Social Security Administration to stabilize staffing at 63,000 and continue to invest in automation, thus ensuring high quality service to our public.

Our legislative agenda includes several initiatives which will encourage the profession of health services in managed care settings. We believe managed care is the best means of assuring quality service and appropriate care for medicare and medicaid beneficiaries.

We are also proposing changes to the Medicare program which will save $5.5 billion. These changes are designed to make the medicare program a prudent purchaser of services, and to assure that current inequities in physician payments are not built into the new reimbursement system to be implemented in fiscal year 1991.

With these proposals, Medicare expenditures will increase by 4.6 percent between 1990 and 1991. Without them, the inflation rate of this program would continue at more than double that rate or 9.9 percent.

You will note that in our budget, we are proposing to finance some of the services we provide through user fees. For example, my request includes $510 million, an increase of $312 million over the 1990 level, for survey and certification of health facilities to ensure the safety and the quality of care provided.

Following the lead of the Congress in the Clinical Laboratory Improvement Amendments of 1988, we propose funding all activities, including those previously funded by Medicaid, through user fees.

Lastly, and perhaps most importantly, our budget honors the 1983 bipartisan promise to our citizens that there will be sufficient funds for Social Security today and in the future.

Further, we propose additional protection for future beneficiaries through a plan which would end the current practice of using the reserves to mask the size of our deficit.

So let us not contemplate any sort of action which will ultimately endanger the economic future of our children and our grandchildren.

That completes my statement, Mr. Chairman, and I will be pleased to respond to your questions.

[The information follows:]

Mr. Chairman and Members of the Committee, thank you for inviting me here today to discuss the President's fiscal year 1991 budget proposal for the Department of Health and Human Services. We are requesting $464 billion in outlays, an increase of $27.5 billion over current year spending.

Our appropriation request for HHS programs considered by this Committee totals $136.8 billion. This is $12.3 billion over fiscal year 1990, or an increase of almost 10 percent.

This budget reflects the President's and my own priorities for the Department. I am proud of this budget and look forward to working with the Congress for its enactment.

As you and I are aware, several of our goals for 1990 were not fully achieved, a prime example being the expansion of Head Start. This year, we are seeking an unprecedented increase of $500 million for the program, which will open new doors of opportunity to an additional 180,000 children and their parents. I want you to know that I share President Bush's enthusiasm for this expansion. In the spirit of cooperation, we must work together to get every dollar of this increase. We were also disappointed that, last year, funds we received for the homeless, the Human Genome Project and AIDS were less than requested.

In each of these areas, I am back this year asking for more, and I hope that, together, we can bring about these increases.

For fiscal year 1991, the Department's efforts to improve the health and well-being of the American people will emphasize my major goals -- helping children, strengthening families, investing in the future through enhanced biomedical research, improving access to health care, promoting good health, fighting AIDS, combating drug abuse, prudently managing our large entitlement programs and increasing the quality of services provided to the public.

Let me take this chance to go over some of the highlights of my request:

For the Head Start program, we are asking for a 36 percent increase, bringing the total for Head Start to $1.9 billion. The expansion of Head Start is a key ingredient in assuring that all our children start school ready to learn, one of our national education goals. The addition of $500 million will allow 180,000 additional children to receive the learning, skills and confidence Head

Start offers. I hope that Congress shares this goal and will support this critical increase. Every eligible disadvantaged 4-year old deserves the opportunity to enjoy a Head Start experience.

As part of our expanded support for families in need, we are requesting the full authorized ceiling of $1 billion for the new Job Opportunities and Basic Skills Training Program. The education, training and work activities provided under the JOBS program are essential for restoring dignity to families on AFDC and readying them for the employment opportunities this decade will bring. Our request will enable the 23 states without JOBS programs to implement them, as required, by October 1990.

To provide additional assistance for parents entering the workplace, support for JOBS and AFDC-related child care will increase by $283 million for a total of $489 million. Increased availability of child care services will allow more AFDC parents the opportunity to complete education, training and work programs successfully, and move themselves and their families permanently off welfare and out of poverty.

To bring about much needed reforms in the areas of child welfare and foster care, we are requesting a $47 million increase for Child Welfare Services. This 19 percent increase will help communities to manage increasing and more difficult caseloads. Additionally, we are proposing a 10 percent limitation on annual increases in Foster Care administrative costs. This limitation will keep these costs in check, but will not interfere with payments to foster families or training of parents and staff.

Again this year, the President and I are making good our promise to help America's homeless. We are requesting $233 million, $27 million of which was provided in fiscal year 1990. Last year, the Congress was unwilling to meet our request in this area. This year, we hope HHS health care and community service programs targeted at our homeless population will be funded at the levels of our request.

On January 24, in announcing his new National Drug Control Strategy, the President renewed his commitment toward demand reduction efforts. To address this and other HHS anti-drug abuse activities, we have included $1.7 billion in our request. This level of funding will allow increases in almost all aspects of this Department's efforts to win the war on drugs. It will also provide for new initiatives, including a $50 million community

prevention grant program and a $6 million project providing non-medical services for infants born addicted to crack. The American public is demanding much more action in preventing and treating drug abuse, and we are responding to this call for help.

As a part of this budget, our efforts for increasing access to quality health care will focus on disadvantaged pregnant women and their infants. Clearly, the fact that the United States ranks near the bottom of all industrialized Nations in infant mortality is disgraceful.

To concentrate on improvement in this area, our budget includes an increase of $63 million for PHS programs aimed at reducing adverse pregnancy outcomes and improving infant survival. It also fully funds the enacted Medicaid expansions for pregnant women and their children with incomes at or below 133 percent of poverty.

Death rates among minorities for heart disease, cancer, stroke, AIDS and other disorders are far greater than those of the population as a whole. Correcting the disparity in health status between minority and non-minority populations remains one of my highest priorities. To this end, we are seeking $117 million for a new initiative to improve access to health care for low-income minorities. This will include increasing the number of minority health professionals and initiating innovative community-based approaches to recruiting minorities into health careers. We will also develop new strategies for delivering needed health services to our minority populations.

In addition, the budget includes $357 million for access to care for rural Americans. Ninety-two percent of this amount, or $327 million, will be spent on services for rural communities. This includes continuation of those activities initiated by Congress last year for disease prevention and information outreach. $30 million is earmarked for research on the special conditions impeding access to quality care in rural settings.

We also plan to spend $9.4 million to support ADAMHA research projects and services which specifically focus on mental health services in rural areas.

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National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration.

Included in this increase is a major expansion for the Human Genome Project. This research is expected to have a profound effect on our ability to treat the more than 3,500 diseases of known genetic origin. The project was recently ranked by researchers as the number one Federally-funded major science initiative, surpassing even the Super Collider. It must remain one of our highest priorities. We are planning an increase of $48 million over the $60 million Congress provided in fiscal year 1990.

To begin the much-needed infrastructure repair of the NIH campus, I am requesting $89 million. We can no longer continue to ignore the fundamental needs of our researchers; facilities must be well maintained and renovations must occur.

Concerning AIDS, we must work until our efforts match the threat of this disease to our society. In fiscal year 1991, we propose to spend $3.1 billion on AIDS. We are requesting $1.7 billion for HIV and AIDS-related activities of the Public Health Service. This $109 million increase will be used for continued research, education, epidemiology and investigation of drugs. In addition, there is a $780 million increase for Medicare and Medicaid services for AIDS and HIV infected individuals.

$110 million is also included for the newly established Agency for Health Care Policy and Research. This amount includes funds for an expanded Medical Treatment Effectiveness Program. The Effectiveness program is a comprehensive effort to learn which medical procedures are most effective for specific health conditions. Effectiveness research is a long-term commitment toward improving the quality of medical care and reducing unnecessary treatments.

I am committed to ensuring the quality of service provided to the public through the large entitlement programs administered by this Department -- Social Security, Medicare and Medicaid. In fiscal year 1991, we are requesting increases for the Social Security Administration and the Health Care Financing Administration which will enable us to continue managing these programs efficiently and effectively.

The budget includes full funding for Social Security, Supplemental Security Income and Black Lung benefits. In addition, we are requesting $4.2 billion, an increase of $330 million, for the

Social Security Administration to run these programs. These funds will allow SSA to stabilize staffing at about 63,000 and continue to invest in automation, thus ensuring high quality service to our public.

Our legislative agenda includes several initiatives which will encourage the provision of health services in managed care settings. We believe managed care is the best means of assuring quality service and appropriate care for Medicare and Medicaid beneficiaries.

We are also proposing changes to the Medicare program which will save $5.5 billion. These changes are designed to make the Medicare program a prudent purchaser of services and to assure that current inequities in physician payments are not built into the new reimbursement system to be implemented in fiscal year 1991. With these proposals, Medicare expenditures will increase by 4.6 percent between fiscal year 1990 and fiscal year 1991. Without them, the inflation rate of this program would continue at more than double that rate, or at 9.9 percent.

You will note that in our budget, we are proposing to finance some of the services we provide through user fees. For example, my request includes $510 million, an increase of $312 million over the 1990 level, for survey and certification of health facilities to ensure the safety and quality of care provided. Following the lead of the Congress in the Clinical Laboratory Improvement Amendments of 1988, we propose funding all activities, including those previously funded by Medicaid, through user fees.

Lastly, and perhaps most importantly, our budget honors the 1983 bipartisan promise to Americans that there will be sufficient funds for social security today and in the future. Further, we propose additional protection for future beneficiaries through a plan which would end the current practice of using reserves to mask the size of our deficit. Let's not contemplate any sort of action which will ultimately endanger the economic future of our children and our grandchildren.

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Thank you very much. I will now be happy to answer any questions you have about our request.

Mr. NATCHER. Thank you, Mr. Secretary.

Yesterday under the direction of our Chairman, Mr. Whitten, we had our overview hearing with the Secretary of the Treasury, the Director of the Office of Management and Budget, and the Chairman of the Joint Economic Council, and during the hearings, Mr. Secretary, it developed that since 1980, $2,612,000,000,000 has been appropriated by the Congress and spent by the Department of Defense.

I asked the staff while you were making your statement to give me just a round figure, if possible, as to the amounts that have been appropriated since 1980, not including trust funds for your department, and it's in the neighborhood of $860 billion.

Mr. Secretary, that is not too much. Also, during the overview hearings, it appeared and it was developed that for education we have in the current budget $24.1 billion for education. And for education down through these years, we have appropriated about $199 billion.

We believe on this committee, Mr. Secretary, that if you take care of the health of your people and educate your children, you can continue living in the strongest country in the world.

When I was first elected a Member of this committee, we had $73 million Mr. Secretary, for NIH. Mr. Conte and I and the other Members of this subcommittee down through the years, with the assistance of your predecessors and those in your department, have brought this figure for the National Institutes of Health up to $7,576 million for the fiscal year 1990, and if I had my way, Mr. Secretary, today it would be $10 billion

We have done a little better as we have gone along down through the years with health and maybe in some of the other departments.

As you pointed out, in some instances we have not appropriated the entire amount requested, but we bring health up and education up, and also other sections for the Department of Labor.

And Mr. Secretary, again, I want to thank you for an excellent statement.

Mr. Conte, I yield to you.

LOW-INCOME ENERGY ASSISTANCE

Mr. CONTE. Doctor, this is the second year in a row that we have seen minimal funding for low-income energy assistance, and now with the cold weather, with the record-breaking cold weather in December, we are finding out that states are running out of low-income assistance at the level where we have provided it in the appropriation bill.

Many families have used up all of their benefits already, and there is simply not enough to go around this year.

Amidst the winter freeze waves, this budget comes out and proposes a whopping $343 million cut this year. I was absolutely stunned to learn, Doctor, that my good friend, that you went to OMB; and if that is true, you were against a hundred million dollars to add on to your initial request of a billion dollars for LIHEAP. And I am completely at a loss in understanding this action. It's the poor that need the help most with their skyrocket-

ing heating bills. LIHEAP is their chief source of assistance, and you know that freezing is hazardous to your health, Doctor.

Is this Administration prepared to throw these people out in the cold, choosing between heating—and eating?

Secretary SULLIVAN. Thank you, Mr. Conte, for that question.

Certainly it's not our intention that any of our citizens should go without needed funds for protecting themselves against the elements, but there are several things about this program that we are concerned with.

The first is that when this program was first enacted a number of years ago, it was intended to be a temporary program, that was during the time of the oil embargo, of course, which has long since passed.

The second problem we have is that it's a program that has such a disparate effect across the country.

We believe that this really is a program that is more appropriately administered by our States, which is why we have concerns for this continuing as a Federal program. What we have noted as we have monitored this program is the fact that, I believe, more than half of our States transfer funds out of the LIHEAP grant into their Social Services Block Grant and other programs, indicating that they are not really utilizing or needing all of those funds.

The converse side of that is, of course, that States have the capability of transferring monies out of their Social Services Block Grant funds, up to 10 percent, into the LIHEAP program, and none of the states have done that.

It would appear as we monitor this program that the need for the program overall is not as great. Finally, we were concerned, with the record cold that did occur back in December, and the escalating costs of heating oil.

But we also have been pleased to note that the month of January has been warmer than normal, and the projections seem to indicate that that will continue to be the case.

In addition, the cost of heating oil now is lower than it was on December 1, so that escalation in the cost has now, at the wholesale level at least, been corrected.

Those are the kinds of observations that lead us to believe that this is a program that would best be administered at the State level rather than at the Federal level.

Mr. CONTE. Well, I could agree with you on some of the things you mentioned, but the trend has been that fewer and fewer States are transferring less money, and many energy States like my own, Massachusetts, don't transfer any funds at all.

Furthermore, the authorizing committees are considering eliminating the provision which allows transfer of funds, and so the issue still remains, how can we get more benefits out there to the people who need it the most?

And my State in particular, our Governor has done such a terrible job, we are in a colossal financial mess up there. You can't get two nickels to rub together. So we are out of money.

There is a headline in yesterday's papers, "Crisis Looms for Western Massachusetts." But I am worried about the poor people out there that are running out of money, and hopefully, we got to all pray that the weather is going to stay pretty calm and not get

too cold in February and in March. We can have some real bad weather up there.

PUBLIC HEALTH SERVICE REORGANIZATIONS

On another subject, Doctor, in last year's conference report to the Labor/HHS Bill, there is language that states, "No funds are provided or are to be used for reorganization of the Public Health Service regional offices prior to approval of a reprogramming request."

Do you intend to comply with that language?

Secretary SULLIVAN. Yes, Mr. Conte.

It was brought to my attention a few days ago that there was some concern about a plan of my Department for reorganization. No plan has yet come to my attention. I think members of my staff are looking at how we are organized and how we are operating, and part of that review includes how our regional offices operate.

But no plan has yet to come to my attention, and if it does, you can be sure that I will comply fully with Congressional intent.

NATIONAL INSTITUTES OF HEALTH DIRECTOR

Mr. CONTE. Okay.

I have been concerned, and I am sure the Chairman has been concerned, about the NIH directorship which has been vacant for quite some time. Can you bring us up to date? Are we getting any closer having a director?

Secretary SULLIVAN. I think we are, Mr. Conte. Let me say this about the NIH Directorship. This clearly is one of the key positions in our Department because as I noted in my statement and certainly as I agree with Mr. Natcher's accounts, this is really an outstanding institution. It has made many contributions to advancing the health care of our citizens, contributions that we really have almost gotten to take for granted.

I will give you a quick example of one. When I was a medical student at Boston University back in the mid 50s, I took care of patients with paralytic polio during the epidemics of 1956 and 1957 in the summers there. That was a labor intensive activity; to change the linen of the patients, for example, in the iron lungs would require several nurses, one or two students, a resident, et cetera. If you were to project from 1956 to 1990 what we would be paying for the care of patients with paralytic polio, if we didn't have a polio vaccine, it would be astronomical.

During the same time I was taking care of those patients, Dr. Thomas Enders at the Microbiology Department at Harvard Medical School with a grant from NIH for $53,000 was finding a way to grow the polio virus in the laboratory. He discovered a way to grow the virus on kidney slices and, of course, he got the Nobel Prize for that, because that was the key discovery which then enabled us to grow the virus and for Jonas Salk and Sabin to develop their vaccines.

Polio is now virtually gone from our country, and now we are even projecting the possibility of eradicating polio around the world.

For that modest investment of $53,000, we are saving hundreds of thousands of dollars every year. This does not even include the fact that we have citizens who are staying healthy and, producing incomes rather than being in rehabilitation hospitals; citizens who might otherwise have to go to orthopedic surgeons for tendon transplants because of withered limbs, et cetera.

I think you can see from just that one discovery, funded by NIH, we have improved the health of our citizens, as well as helped our economy.

We want to do everything we can to preserve the strength and the growth of NIH for those obvious reasons. Because we have had difficulty in attracting top flight persons to the Directorship at NIH, I have convened a special committee of outstanding researchers and business people from the private sector to help advise me on ways to make that position more attractive.

I have discussed this with the President, and he is aware of this issue. We will be coming back, I am sure, not only to the President, but also to the Congress, once we have gotten the full benefit of the thinking of these outstanding individuals, to really do what we need to do to make that more attractive.

We know that among other things, the salary is very low. We have a three or four fold difference in the salaries that we pay our senior people at NIH and what they could earn in the private sector, not only in the pharmaceutical companies, but also in our universities and so forth.

There are also some other problems that I want to alert you to where we will need your help and that of the Congress, and that is inadvertently over the years, the authority of the NIH Director to really plan for the development of the budget and direction of NIH has really been eroded by such things as creating additional institutes at NIH where I know the feeling has been that if you create an institute, it will advance work on the particular disease more rapidly.

What has happened? We have created Institutes without expanding the number of personnel, so we have caused a hemorrhage from within because as we have created new institutes, we have then parasitized the existing institutes to populate the new institutes.

NIH has a terrible problem with full time equivalents (FTE), and as I indicated in my statement, we haven't even kept up with the facility in terms of modernization.

There are a number of things that we need to do to enable us to attract the top flight kind of person. That person needs to be a scientific leader as well as someone who has strong administrative capabilities.

Hopefully, within a few weeks we will be able to announce that we have attracted someone to head this very important Institution.

Mr. CONTE. I appreciate that, and I appreciate the answer. I have consumed my 10 minutes, but when I get my second turn, we will get into my senior biomedical reserve service legislation.

Thank you, Mr. Chairman.

Mr. NATCHER. At this time, Mr. Secretary, I yield to our friend Neal Smith of Iowa, who not only serves on this committee, subcommittee with distinction, but he is chairman of the subcommit-

tee that appropriates the money for the Departments of State, Justice and Commerce.

Mr. Smith, I yield to you.

NATIONAL INSTITUTES OF HEALTH ORGANIZATION

Mr. SMITH. Mr. Secretary, the Chairman and I have been on this subcommittee 24 years, and I want to say to you, you are lucky to have the Chair and the ranking member, Mr. Conte, primarily concerned with your funding for these departments, because they have been very sympathetic to your needs.

As the Chairman indicated, we remember when funding at NIH was only $73 million. That was some years ago. But there are always unmet needs in the areas you are dealing with. And always changes that need to be made.

And I was very interested in your observations concerning the institutes. My observation has been when we create new institutes in large measure, we just divided up what was being done. There is so much overlap anyway, and in too many instances, I am afraid, the new institute was created because somebody wanted to get their name on a bill saying they had created a new institute, when we didn't increase the ability to deal with the problems out there.

And I interpreted your answer to mean that you may think it is time to think about less numbers of institutes. Is that right or not?

Secretary SULLIVAN. I am not sure that I want to say that. I would certainly say that we don't want any more institutes, because the fact is——

Mr. SMITH. There is a great overlap between institutes?

Secretary SULLIVAN. Yes. Research really is going on, so that it is not that creating a new institute means that we are now going to be exploring a new area of research.

As you know, there is a lot of cross fertilization that goes on in research. For example, with the new Deafness Institute that has been created, and for which we will be swearing in the Director, Dr. Snowe from Pennsylvania, next month. That work was going on in the National Institute for Neurological Diseases and Stroke.

There is a lot of cross fertilization. Those individuals who are concerned with the auditory functions of the hearing and balance, et cetera, interact with other neurological people concerned with Alzheimer's, et cetera.

One of the strengths of the research environment is a cross fertilization that occurs when scientists talk to each other.

So in a sense, when you create divisions, you may really get less of that cross fertilization. We certainly want to continue to get the resources that are needed to ensure that the work will go on.

In no way do I want to suggest from my remarks, that we are not interested in furthering that. That is not the case. But we simply have administrative costs created for us, and it makes the direction of the Institutes more difficult for the NIH Director overall.

DONOR REGISTRATION

Mr. SMITH. Now, I want to talk to you about a couple of things that I think—we always find things that need to be done.

With regard to an increasing number of diseases and the treatments, a blood analysis is needed so we can get donors, find people who will contribute parts or blood or whatever it is, what do you think about the bank of information we have as to the numbers of people that might be available to contribute to a particular disease or treatment?

It is very inadequate; isn't it?

Secretary SULLIVAN. Yes, indeed, it is. We have several data banks of people in registries for different kinds of organ donation. One of the areas that has gotten a lot of attention recently, of course, has been the Bone Marrow Donor Registry. I believe our budget includes some $4 million to support developing a larger bank of individuals for such transplants.

Mr. SMITH. Well, isn't it about time we have some kind of a national bank where anybody that wants to goes and volunteers and make a detailed analysis of their blood, and have that available in banks so that no matter what kind of treatment or problem comes up, it would be available?

I understand they are charging $25 per capita for these when someone needs treatment to get the blood analysis, and that is almost prohibitive for one patient.

Secretary SULLIVAN. Yes. In fact, I think it is $75 for the testing needed for potential bone marrow donors.

That touches on one of the areas that we haven't yet been able to work out. That is the $4 million which we requested is for administrative costs of operating a data registry of individuals whose antigenic types are known for donation.

Indeed, a major issue that you obviously are touching on now is the cost of actually performing the test, which, indeed, could be considerable.

Mr. SMITH. If we had a national registry and a national program to cover various blood needs, it could be done rather cheaply per capita.

Secretary SULLIVAN. We would need to calculate that estimate. I think that one of the problems we face when it comes to bone marrow transplants is numbers. The experts tell us we need to have a reasonable chance of having a donor who is sufficiently compatible with the potential recipient, perhaps as many as 20,000 potential donors.

Mr. SMITH. Well, if you had several million on a computer, you would find out who they were rather fast.

Secretary SULLIVAN. Oh, yes. No question about it. The technology is there. We have that capability. The real issue right now, of course, is the cost of the test. But we have the program in place in terms of the computer capability of recording that data.

DRUG EDUCATION FOR EXPECTANT MOTHERS

Mr. SMITH. Another thing about pregnant women who are addicted to drugs and other substances, my observation; and I have talked to a number of people about this, that deal with this, perhaps most women, I use that most advisedly, most women that are taking drugs and other substances don't realize that what they

take through their mouth or into their body is going right into that baby. It is an education program.

Do you agree with that?

Secretary SULLIVAN. Oh, yes. That certainly fits into one of our strong priorities for our health promotion/disease prevention program.

Mr. SMITH. Well, there is nothing in this society we have today that education that educates the general public faster than television, through my observations. We need some television programs, don't we, that specifically zero in on this, telling mothers and potential mothers that whatever you take into your body, if you become pregnant, is going into your child, you are going to affect your offspring.

Secretary SULLIVAN. Yes. There are some efforts that are underway, though clearly I would agree, it really could be beneficial to expand them significantly.

The effort that I would like to cite here is the private effort from the Partnership for a Drug Free America, that has actually committed itself to raising $365 million annually, usually in donated advertising, from the major TV networks. The former chairman of Johnson and Johnson is heading that up, and we have worked with him, as has our drug czar, Bill Bennett.

Clearly, an educational effort like this needs to be continued and expanded because of the fact that it does take long and sustained effort for that.

EDUCATION

Mr. SMITH. Now, I want to touch on another subject I wouldn't bring up to you.

We hear about these great deficiencies in our education system.

One of them is in the lower grades, preschool and the lower three or four or five grades, we are not doing enough there, and the other is that we just seem to never get around to doing nearly as much for those who need to prepare themselves for adult life if they are not going to college as we do if they are going to college.

Are these two areas greatly deficient in our education system?

HEAD START

Secretary SULLIVAN. Yes. I think there is no question that we really are falling behind in our efforts to prepare our young people to be productive citizens and leaders.

Mr. SMITH. These two are not unrelated.

Secretary SULLIVAN. Oh, I agree with you. That is one of the reasons that we are very pleased that the President has proposed to increase our Head Start budget by some $500 million because of his commitment to have this program grow until all eligible four-year-olds can have a Head Start experience or Head Start-like experience.

We are presently reaching about 39 percent of the four-year-olds, but the $500 million increase, which I hope that you and your colleagues in the Congress will give us, will bring us up to approximately 60 percent. We also have 10 of our States contributing some of their dollars to the program. What we would hope is that we can

get the $500 million, bringing us around the 60 percent level, and with added support from the States we might, in future years, be close to reaching that goal of all eligible four-year-olds in the program.

EDUCATIONAL COUNSELING

Mr. SMITH. I think a lot of high schools don't have the education programs that prepare the students for life, if they are not going to go to college. But in addition to that, our counselors aren't doing their job, are they, in many instances?

Secretary SULLIVAN. Well, there are certainly a number of instances we are aware of where counseling has been deficient, or may not have been there at all.

Mr. SMITH. Counselors in many instances take the summer off; they have to keep up every year if they are going to give a good counsel. They don't know where the jobs are or the opportunities are if they are not going to college.

Many of them are that way.

Secretary SULLIVAN. That is correct.

We have had discussions with Dr. Cavazos, our Education Secretary on this, because as you know, we have within Health and Human Services, responsibility for health professions education for physicians, dentists, nurses and others.

We have a lot of interrelations there, and certainly I would agree with you that we need to do everything we can to strengthen our public school system starting with the prekindergarten right through high school.

Mr. SMITH. I am sure this is not typical, but one student that came, made an application for military academy. I asked him what he was going to do if he didn't make the grade and he didn't really know. And I said, well, didn't your counselor tell you about other ways to get into the military field, if you want to, or other things you can do?

And the sum and substance of it was, well, no, really, after talking to the counselor, he had—I had indicated I wouldn't be able to go to college, and that was about the end of the interview.

There is still a lot of this going on. I know some counselors are very good, but there are a lot of them that that is all they are there for, is to tell you how to get into college.

Secretary SULLIVAN. Well, there is no question that we really are losing out on opportunities to help our young people prepare themselves for being useful citizens. Of course, it hurts our nation in terms of the contributions they could make as professionals, as workers in our society. Secretary Dole in the Labor Department, I am sure, has probably already told you of her great concern that our growth of people entering the job market now is only around one or two percent.

Mr. SMITH. There are a lot of training programs that are available to many of these people if they just knew about them.

Secretary SULLIVAN. I agree with you.

Mr. SMITH. I think I have used my time.

Mr. NATCHER. Mr. Secretary, on this subcommittee we have a gentleman from the State of Michigan by the name of Carl Pursell,

and no member of this subcommittee works harder on this bill than Mr. Pursell.

When we marked this bill up, matters pertaining to our department in its entirety were of great concern to this member, and especially, Mr. Secretary, when we reached the point of nurse training and scholarships. He said, Mr. Chairman, are you sure about that amount, and as a general rule, he gets his way.

I yield to Mr. Pursell.

HEALTH EDUCATION

Mr. PURSELL. Thank you, Mr. Chairman. Keep going. You are doing fine. Thank you.

I am very honored to have you here, Mr. Secretary. You have visited my district already. I had the pleasant occasion this morning to have breakfast with the Secretary of Veterans Affairs, Edward Derwinski. I think that was a great appointment. His background is from the University of Michigan, so I think he will do an outstanding job for this Nation. He served as the HCFA Administrator for four years, which is the longest in our history, because that is an enormous responsibility under your leadership and direction.

So I congratulate you for that nice appointment.

Secretary SULLIVAN. Thank you.

Our Surgeon General designate, Dr. Novello also received her public health degree from the University of Michigan as well.

Mr. PURSELL. That Massachusetts, Kentucky, Atlanta, Michigan connection, Ohio, Maryland connection will serve this nation well.

I just want to comment briefly on Neal Smith's comments this morning.

Neal, I introduced yesterday elementary counselor bill. I think the counselors are on the wrong end of the system, an elementary system really doesn't have the time to look at a good new nutritional program or the health program or the whole problem of health, the whole problem of literacy, drugs, and all of the others related to it, but our health community really doesn't have a component in any of our elementary systems at all. They may even have a part time nurse available and that is about it on their budget.

And most of the curriculum classes really doesn't have a structure for preventive health efforts, and that is really, I agree with Neal, that that is really where that effort is.

I think with your development of a new policy committee, if there is any effort, any initiative, to look at, to integrate health community into the elementary community, gee, it would be a big savings of investments when we are looking at the cost containment, health containment of our nation's high cost of health.

I think obesity and all of those issues really start in the elementary system, and our young—we did a study two years ago, I did with NIH study. It is probably sitting on a shelf somewhere of a fourth grade class that had a nutrition program and exercise program built in with the fourth grade class with a control group and they are way ahead of their families in terms of nutrition and changing their health habits, but it was only a study, and I ven-

tured a guess that that study is probably sitting somewhere in the NIH on some shelf, and it has not been disseminated very well.

But I think Neal is right on track on that. Maybe you would care to comment.

Secretary SULLIVAN. Yes. I couldn't agree with you more enthusiastically. Our Public Health Service under the direction of Dr. Mason, our Assistant Secretary for Health, has established goals for the nation's health for the year 2000 (health 2000). These include, among other priorities, improving the scientific literacy of our society, including their knowledge of human biology and health.

What we propose specifically in those objectives, is that instruction throughout the public school system at all grades includes instruction concerning human biology and health. Our objective is to make sure that our citizens are enlightened about ways that they can promote and protect their own health. We see this as a real priority.

Because, as you know——

Mr. PURSELL. Could you design a model curriculum piece that could go into the classroom that teachers could pick up that has, maybe not so scientific approach, but more, I will say, common sense approach? I taught for some years in elementary, secondary, a school administrator, a teacher is so busy, Dr. Sullivan, that they need sort of a project development form, a curriculum piece, that could fit into their schedule on nutrition, physical fitness, exercise, they don't even teach exercise much, whether it is jogging or gym work or on a daily basis, so that whole area needs a real common sense model that could be designed with maybe our counsel on physical fitness and our President's counsel under your direction, too.

Secretary SULLIVAN. Yes. We are working to develop such a model curriculum, because we believe that it will have tremendous benefits.

Mr. PURSELL. Jim Mason will be directing that?

Secretary SULLIVAN. Yes. Along with Dr. Mike McGinnis.

Mr. PURSELL. Since they were recommended by us, and see if we could relate that to what you are trying to do.

Secretary SULLIVAN. Fine. We would be very pleased to have those.

AIDS FUNDING

Mr. PURSELL. My other area of interest is on AIDS budget. That is really skyrocketing and I was looking at a chart from the Centers for Disease Control here just this month and I commented to the committee last year that I was concerned that we were spending more money on AIDS than chronic illnesses, and they list all the states here, Centers for Disease Control. Michigan ranks number one in trying to kill premature deaths in cancer, heart, lung, hypertension and all that.

Kentucky ranked fifth in the nation. Bill Natcher, you ranked fifth. Michigan is first, Ohio is fourth, chronic illnesses, to Louie Stokes' state, Massachusetts, 26, pretty good record.

So we have got a pretty good record. But our chronic illness efforts have not been funded in terms of a high priority, and so the AIDS money now is, in all due respect to AIDS, and we have an economic—well, I want to say epidemic problem, and I realize some of the AIDS money is going into blood and other areas that could have impact on other research across the board.

But, I really think it is time that the committee take another look at our priorities, because the chronic illness area is getting squeezed down in terms of Federal dollars, and one area has been strong, done very well, but I think we have got to take another look and revisit that whole area.

And I know it is sensitive, but the Michigan department of health is spending more money on AIDS than they are on the chronic illnesses and here we rank in Michigan, number one. That is our problem in Michigan and I will address that with the Michigan public health department. But they get their money from this committee basically, and I think that needs to be refocused to some extent, put it in balance.

I am not saying go to zero funding on AIDS, I think it is a critical issue, but I think it needs a better balance.

Secretary SULLIVAN. I certainly understand your concern, Mr. Pursell.

In our NIH research budget, cancer research is still number one in terms of the dollars that we spend.

Mr. PURSELL. But the AIDS is $3 billion.

Secretary SULLIVAN. That includes money for treatment as well as for research and prevention, including Medicare and Medicaid programs.

Mr. PURSELL. But it is comprehensive AIDS money, and if you are going to increase your AIDS budget another $109 million, which will take it to $1.7 billion, that is more than you are spending on cancer, heart, lung, hypertension and all the other chronic illnesses; is it not?

Secretary SULLIVAN. Well, the $1.7 billion is the research and prevention budget for AIDS at NIH as well as in the rest of PHS. The cancer budget is still larger than that. We are concerned about the balance, including our attention to chronic diseases.

The reason for the emphasis on AIDS research at this time is that this is a problem which is growing and threatens to continue to grow at a rapid rate if we don't get control over it. In contrast to most chronic diseases, one of the issues with AIDS is the fact that it is communicable.

We feel that we have an opportunity, by focusing the resources that we are on AIDS, to learn more about how this disease is spread so we can find ways to interrupt that spread as well as develop treatments. We are spending $1.7 billion now with the expectation that the results will save us down the road, not only in terms of dollars, but also in lives. The situation is a rough analogy to the polio situation that I alluded to earlier.

AIDS FUNDING

Mr. PURSELL. I understand.

Secretary SULLIVAN. It is a situation where we have a scientific opportunity to really move in and solve a problem that will save us tremendous human suffering as well as dollars down the road.

So hopefully in a few years we won't need to be devoting those kinds of resources to AIDS.

Mr. PURSELL. Well, we can apply that argument to cancer, heart, hypertension, diabetes. Those are areas that need a lot of investment too in terms of prevention, because we are getting more premature deaths in those programs than we are in AIDS.

Secretary SULLIVAN. I fully agree.

Mr. PURSELL. So it needs balance. We agree on that.

Secretary SULLIVAN. Oh, absolutely. Right.

Mr. PURSELL. Thank you, Mr. Chairman.

Mr. NATCHER. Dr. Sullivan, long before I met you I knew that you were the first president of the medical school at Morehouse College, and that you had developed it, and it was an outstanding school, and due to the fact that I would talk to my friend Louie Stokes every once in awhile, no member has served on this committee that has worked harder.

And Dr. Sullivan, when we mark this bill up, you can make sure that Louis Stokes is present, and sees to it that the adequate amounts are appropriated, and at this time I yield to you, Mr. Stokes.

MINORITY HEALTH

Mr. STOKES. Thank you very much, Mr. Chairman. I appreciate your very kind words.

Mr. Secretary, let me begin by joining with my colleagues in the accolades that were extended to you this morning for the outstanding job that you are doing as Secretary of Health and Human Services.

I have, of course, known you as has the chairman, for many years. I have admired you and worked with you on many of the initiatives that this subcommittee has in effect put into legislation, most of it at your urging, long before you even became Secretary of Health and Human Services.

We are very proud of the job that you are doing. I was particularly proud of something that was mentioned by Mr. Conte earlier this morning, and that was your aborting the attempt by R.J. Reynolds to target cigarettes towards the black community. Thank God you were around and that you took the strong forceful stand that you did. They backed down. You were able to stop this.

I think it might be important for our committee to understand the magnitude of this problem, and how minority populations are targeted for additional deaths from cancer and alcoholism and other diseases.

Would you care to address the problem?

Secretary SULLIVAN. Yes. Thank you very much, Mr. Stokes, and certainly I want to thank you for the leadership that you have shown over the years in efforts to improve the health of our citizens, including our poor and minority citizens, and certainly I value your comments very much.

We are facing a problem when it comes to the health status of our minority communities. As you know, one of my predecessors, Secretary Heckler, issued a report in August of 1985 that showed that we had in the nation every year some 60,000 excess deaths in our minority communities that would not occur if the health status of our black, Hispanic and Native American communities were equivalent to that of the white community. Among those major reasons for this difference, were deaths due to cancer and heart disease. As you know, as a nation, our number one cause of death is heart disease, and cancer is number two.

When you look at the death rate in the black community from heart disease, it is about 37 percent higher than that of the white community.

Cancer deaths are some 34 percent higher in the black community than in the white community. A large segment of the cancer deaths are due to lung cancer, the number one cancer, and, of course, that is clearly related to smoking.

A large number of deaths from heart disease are also related to smoking and the negative effects it has on circulation and on the heart.

We know irrefutably, that the number one preventable cause of death in our country is smoking.

So, when we say that we are trying to improve the health of our citizens, we need to have, in addition to our marvelous medical technology, an enlightened citizenry regarding the things that they can do to help maintain their health. Of course, one of those things is to stop smoking.

We now have knowledge which was unavailable in former years, when the tobacco companies used the excuse that we didn't have the data or we didn't know, et cetera.

Now, we know; no question about it. And to continue to push these products when we now know the death and disability resulting from them, I think, is unconscionable.

Clearly, that is what led me to speak out. The fact is, black Americans have a life expectancy in our society of six to eight years less than whites. Average life expectancy for black females is 74 years, versus 79 years for white females.

For black males, it is even shorter. A large amount of that is due to deaths from preventable causes. If we are going to really meet our goal of improving the health status of our citizens, as well as reducing health care costs, prevention and health promotion have to be important components of that effort. That is where we need to have our citizens working with us in improving our health behavior.

Those are the factors that led to those comments, and we intend to continue speaking out, trying to educate our citizens about things that they can do and should be doing to improve their own health.

MINORITY HEALTH CARE PROFESSIONALS

Mr. STOKES. That leads me then into the next question.

Your budget includes $117 million Public Health Service wide initiative to improve the health status of minorities. $107 million of

these funds will be for providing health care or training in the health professions to minority populations.

Now, this committee, I am sure, is aware that while black Americans represent about twelve percent of the U.S. population, only two percent of medical school faculties are black professors. So I wonder if you would want to talk about this initiative a little bit.

Secretary SULLIVAN. Yes, Mr. Stokes.

We are certainly very pleased to work with you and your colleagues here in the Congress. Your leadership on this effort is appreciated because improving the health of our citizens is a multifaceted effort.

One of those components has to be an adequate number of health professionals, to make health care available and accessible to our citizens. When we look in the city ghettos, as well as in our rural areas, we see that those are the areas where we don't have an adequate number of health professionals. We think that an initiative such as the one that you have sponsored in the Congress is most appropriate.

We are, therefore, pleased to be working with you in that effort and, of course, our budget for minority health initiatives of $117 million is designed to work with you on that.

I think there are some minor difficulties that we may have concerning the legislation but we are sure those differences can be worked out. We agree fully with the intent and the principles of that legislation, and we certainly look forward to working with you.

To be sure that we would have this in the budget that we would be submitting to the Congress for 1991, we sat down with the OMB director and got a commitment from him that it would be included. I am pleased to report to you that that commitment has been honored. So we look forward to working with you to implement that effort.

Mr. STOKES. Thank you, Mr. Chairman.

Mr. NATCHER. Mr. Secretary, the next gentleman that I will yield to is not only an outstanding Member of this subcommittee, but he is a chairman of the subcommittee that appropriates the money for foreign aid.

He might not tell you this, Mr. Secretary, but he is more interested in that and the education of our people than he is in some parts of his bill. And I yield to him.

Mr. HOYER. He would be glad to tell you that, I think.

REFUGEE RESETTLEMENT

Mr. OBEY. Thank you, Mr. Chairman, and that leads me to my first question.

Mr. Sullivan, I will not get into the issue of LIHEAP. I understand Mr. Conte covered it.

I simply want to suggest that I agree with everything that I expect Mr. Conte said on the subject.

I would like to talk to you about your refugee assistance. In 1988, we had 77,057 arrivals in this country, and the Administration requested $253 million.

Last year we had 110,000 arrivals, and the Administration requested less than that amount, $210 million for cash and medical assistance. We expect a substantial increase in refugees this year, and yet the Administration is again limiting its request for cash and medical assistance to $210 million.

That means that last year I had to take money out of funds that the Administration requested for refugee resettlement abroad and move some of them over to Mr. Natcher's subcommittee so that we could meet our obligation to our own communities, which the Administration was incurring, but not funding, by allowing increased numbers of refugees in their own country.

My question is, am I going to have to do that again this year, or is the Administration going to finally recognize that it has to quit shifting responsibility for funding refugees, in fact, to local units of government?

Secretary SULLIVAN. Thank you very much, Mr. Obey.

This has been an area that we have followed with interest, because we were impressed by the fact that Congress authorized $1 billion a year over a four-year period starting a couple of years ago for the State Legalization Impact Assistance Grant Program.

Excuse me, Mr. Obey. I was about to describe another program. I now understand that you are referring to refugee resettlement.

Indeed, this is an area that we have been concerned about and discussing in relation to our overview and budget constraints. We have tried to balance competing needs with the monies that we have available.

We feel that there are some responsibilities that our States should have in this effort, and what is requested in our budget is not to provide the total support for this.

REFUGEE SETTLEMENT

Mr. OBEY. Mr. Secretary, since my time is limited, I am going to interrupt and simply make this point. In 1986, the Administration transferred 6.5 percent of the cost to the states for refugee resettlement.

In 1987, they transferred 11 percent. In 1988, they transferred 21 percent. In 1989, they transferred 22 percent.

Do you realize what kind of a local backlash, especially in small communities, the Administration helps create when they increase the number of refugees allowed into this country but do not increase Federal support for those refugees, dumping that responsibility off to the state and local units of government?

And do you really think that is healthy for the country?

Secretary SULLIVAN. Well, of course, a number of the programs that the States administer to provide help for those refugees still use Federal dollars, such as our welfare programs, and others, where there are State funds there but there are also Federal dollars.

Our position is that the Federal Government certainly has a responsibility and is helping, but really it should not be the sole source of funds.

Mr. OBEY. Yes, but what the Federal Government is saying is we are going to let them in and you are going to pay for it. That doesn't make a lot of sense.

You wouldn't like that if you were mayor or county board chairman.

Secretary SULLIVAN. No. But the Federal Government still is contributing to that effort.

Mr. OBEY. The Federal Government has increased the number of entrance by 45,000 people, more than 50 percent over the last three years, and the Administration has requested a reduction in Federal support for that. Now, that doesn't make sense, and that is not fair.

Let me ask you a second point. The 1990 target assistance appropriation included $3.8 million in targeted assistance to be awarded to communities which are heavily impacted by Hmong and Cambodia refugees. That includes districts like mine.

Would you please outline the timetable for the awarding of those grants?

Secretary SULLIVAN. I will have to prepare a response in writing with that information.

[The information follows:]

TARGETED ASSISTANCE GRANTS FOR REFUGEES

The Family Support Administration intends to issue a grant announcement for publication and comments in the Federal Register in early April for the $3.8 million in targeted assistance grants. In accordance with Departmental grant regulations, these will be awarded under a competitive application process. We expect these grants to be awarded in July 1990.

DEPARTMENTAL VACANCIES

Mr. OBEY. Okay.

Is the Assistant Secretary's position for Family Support Administration still vacant?

Secretary SULLIVAN. Yes, that position is vacant, although I would point out, of course, we have an acting Assistant Secretary. In spite of that position being vacant, the operation of those programs——

Mr. OBEY. But it's still vacant?

Secretary SULLIVAN. Yes, it's——

Mr. OBEY. Is the Director for the National Institutes of Health tion still vacant?

Secretary SULLIVAN. Yes.

Mr. OBEY. Is the Director for the National Institute of Health most certainly still vacant?

Secretary SULLIVAN. That is correct.

Mr. OBEY. When do you expect to fill that?

Secretary SULLIVAN. As soon as we possibly can, because I certainly share with you the urgency for getting those positions filled.

But let me say that the Family Support Administration is working well; the regulations that we were required to produce to implement the Family Support Act of 1988, were issued on time.

We have 27 of our 50 states who have come on line with a JOBS program, and we expect that all 50 will be on line by this October 1st, which is the requirement.

We are concerned about those positions being vacant, but in spite of that, because of the good work of our employees in those areas including those acting Directors, the work is being done.

But clearly, we want to get those positions filled as quickly as possible.

Mr. OBEY. And when do you expect the Surgeon General's position to be filled?

Secretary SULLIVAN. Dr. Novello goes before the Senate Committee tomorrow for confirmation; so hopefully, she will be on board in the next few days.

HEAD START SALARIES

Mr. OBEY. Let me ask two more questions. My understanding is that you have been quoted as saying that because Congress provided a $50 million setaside for Head Start last year to increase salaries for Head Start teachers, that the salary increase problem had been taken care of.

Is that an accurate quote?

Secretary SULLIVAN. I don't recall being asked about that, so I clearly don't recall making that statement. But let me comment on the Head Start program, and I will be happy to respond to your——

Mr. OBEY. I would appreciate it, because my time is very brief, if you would confine your comments—do you think that Head Start salaries are adequate for the task?

Secretary SULLIVAN. Yes, I do. We are concerned about expanding——

Mr. OBEY. Then let me make the point that last year, this committee, thanks to Mr. Natcher, who looked kindly upon my request and the request of several others on the subcommittee, we did earmark $50 million for staff salaries. That provided if you take into account the effect of inflation, that provided roughly a 5 percent increase in salary, counterbalanced by a 4.5 percent increase in the consumer price index, which means that we had a net increase of less than half of 1 percent, which, when translated to Head Start salaries, a Head Start teacher making $10,000 a year would have received a double digit salary increase for that year, less than a hundred dollars.

Do you really think that addresses the question of equality?

Secretary SULLIVAN. Well, what we think it does, Mr. Obey, is provide an opportunity for development of skills for people who come into the Head Start program, and an opportunity for upward mobility because I know that one of the other concerns that has been expressed has been turnover.

A lot of that turnover involves people who enter say, the public school system or other places. Our position is that we are not trying to compete with our public school systems, but rather provide a program that gives a service as well as a training opportunity for people working in the Head Start program.

Mr. OBEY. I would move to disagree with the assertion made by the Secretary.

COMMUNITY SERVICES BLOCK GRANT

Mr. OBEY. One last question.

Mr. Secretary, Barbara Bush sent a letter to the Southeastern Association of Community Action Agencies stating, "You are indeed shining examples of the thousand points of light about which George speaks."

What is your request for Community Services Block Grant this year?

Secretary SULLIVAN. We have not made a request for funding for that this year, not because those programs are not important, but only about 12 percent of the budget of those programs comes out of the Community Services Block Grant program, first of all, so they are not critically dependent upon this.

In addition, we do have other programs in our Department that provide resources for those agencies, and I refer to not only our Head Start program and our JOBS program, but other programs as well, not only in my agency, but in other agencies such as the Small Business Administration.

We feel those programs are important, but again, in a time of budget constraints we have to make judgments about the best use of dollars.

Mr. OBEY. Let me tell you what I find funny about the President's budget, and this isn't your responsibility. We are helping NATO build one military base in Italy this year, which will cost more than we will save with the military base cuts which the President has recommended in this year's budget.

And so that means that while there is a lot of hurrah out there in the newspapers about the base cuts, the fact is we are going to spend more on another new overseas base this year, and yet this budget suggests that we cut a program that provides some very important services to some very poor people who very often have no place else to go.

I think that is a backwards budget, and I regret the fact that you have recommended that.

Secretary SULLIVAN. I am sorry, our request is for $42 million I think I said zero before, but I was incorrect.

Mr. OBEY. But as a practical matter, you are trying to eliminate the program. I would simply ask you this: Has your office ever conducted a formal evaluation of the Community Services Block Grant program?

Secretary SULLIVAN. I will have to get a response back to you. I believe we have, but I am not sure.

Mr. OBEY. I don't think you have. And so I would simply suggest that, at least none that I know of. If you have, I would like to know about it. But it appears strange to me that one would recommend the elimination of a program without a formal evaluation of the quality and the success of that program.

Secretary SULLIVAN. I will be happy to get back a response to you on that.

[The information follows:]

COMMUNITY SERVICES BLOCK GRANT EVALUATIONS

The Office of the Assistant Secretary for Planning and Evaluation has supported several evaluations of the Community Services Block Grant (CSBG) program. These efforts include:

1. A study by the Urban Institute of block grant programs, including the CSBG, in 1984;
2. A review by the National Governors Association of the implementation of all block grants, including CSBG, conducted in 1984; and
3. Two studies by the General Accounting Office in 1985 which involved a general review of block grants, including CSBG, and a separate, specific study of CSBG.

Mr. OBEY. Thank you, Mr. Chairman.

Mr. NATCHER. Mr. Secretary, since I have been a Member of Congress, I have served with a number of Members from the State of Maryland; none that ever worked harder, more ably as a Member than Senator Hoyer, none that are more interested in education and health, my friend Steny Hoyer, and I want you to know that.

Mr. Hoyer, I yield to you.

HEAD START

Mr. HOYER. Thank you very much, Mr. Chairman for those very kind words. As one who is interested in education and health, let me say that the Nation owes a great debt of gratitude for your leadership and commitment with respect to these two subjects which are critical to the welfare of our country.

Mr. Secretary, let me say how pleased I am to see you here once again. As a Member of the party other than the President's I am very pleased that you are in the leadership of the Health and Human Services Department.

The President observed in his State of the Union Address that we witnessed a revolution in 1989. Indeed we did, as we observed just yesterday when the Soviet Union adopted a radical change in its constitution.

Cap Weinburger was thrown into a different kind of revolution—one might say, in 1981 to respond to what President Reagan saw as a great need in national defense.

I hope, Mr. Secretary, that you become the Cap Weinberger of 1990 and that you will be in the forefront of the call to arms of our people against poverty and disease and the undermining of our human resources. That battle is going to be critical to our national defense and our national competitiveness in the years ahead. I think you have shown an ability to do that.

Mr. Stokes spoke of your anti-smoking campaign. I think that was a worthwhile and important initiative of yours. I am sure you will be on the forefront of similar efforts.

Let me ask you a couple of questions. Head Start, Mr. Secretary, it's my understanding that if we apply the inflationary rate to Head Start from 1980 to date, we would come up with the $1.886 billion, no more, no less.

That is what the Administration has requested. It's indeed a $500 million increase, and I applaud that.

You indicate that it will fund about 60 percent of the four year olds, those who will be then presumably going to kindergarten. My state has public full access kindergarten. I don't know whether every state has that now or not.

But the program deals with three, four, and five year olds, does it not?

Secretary SULLIVAN. That is correct.

Mr. HOYER. Now, of the eligible three, four and five year olds, do you know the percentage that $1.886 billion will allow us to incorporate in the program?

Secretary SULLIVAN. I know that we have data on the three and five year olds, but I will have to get that back to you in writing.

Mr. HOYER. Okay.

[The information follows:]

HEAD START

With the $1.886 billion requested for Head Start in 1991, it is estimated that 13 percent of low-income three-year olds, approximately 60 percent of low-income four-year olds, and 5 percent of low-income five-year olds will be served. The percentage of low-income 5-year olds not being served by public school kindergarten or other programs is extremely low.

The President's goal for Head Start is to provide one year of participation for all eligible children, preferably in the year before they enter kindergarten. Since all 50 States now provide public school kindergarten, primarly for 5-year olds, the greatest need, and the most potential benefit to be derived, is in serving four-year olds. The long-term goal, then, is to allow at least one year of Head Start to every disadvantaged four-year old in the nation. The 1991 request brings this goal within the program's grasp.

There are approximately 825,000 low-income 4-year olds in the nation, it is estimated that 80 percent of these would want to participate in Head Start. The other 20 percent are either served by other programs, or are not interested in participating in Head Start. With an additional 180,000 four year olds participating in 1991, Head Start will be serving around 60 percent of low-income four year old children.

Secretary SULLIVAN. For four year olds, I think we are presently serving around 39 to 49 percent, and the 60 percent figure is the level for four year olds, we would achieve with the additional $500 million.

We have concentrated on that as our first objective to try and get that prekindergarten group fully up to speed.

Mr. HOYER. And I think that is important, and I applaud your efforts in that regard.

I am convinced, however, Mr. Secretary, that the Department of Education is critically important in this regard. As you well know, Secretary Bennett and Secretary Cavazos make the point that much of that effort is made at the local level.

I frankly think Head Start is a late start—expert after expert tells me that by the time a child has attained the age of about two and a half to three, they have learned a very substantial portion of what they are going to learn in a lifetime.

In my community, we are losing children, black and white. The Dooney Waters story you may have seen was about a young man of six living in a Crack house, completely ignored. What would we need to spend to accomplish the President's long-term goal of providing universal Head Start to all income eligible children and their families?

I am going to support that objective to whatever extent I can, Mr. Secretary. What will that require? And what plans do we have, and in what time frame are we going to try to accomplish that goal?

Secretary SULLIVAN. It would require approximately an additional $500 million beyond our request. And as you know, the President requested last year a $250 million increase, but we only received from the Congress $151 million more.

So, we fell short by almost $100 million of our request last year. We are certainly hopeful that we get the full request this year.

Mr. HOYER. One of the problems we have is the authorized level of funding. Is the Administration urging legislation to increase the authorization level?

Secretary SULLIVAN. Yes, we are.

Mr. HOYER. Mr. Secretary, because my time is limited, let me ask you one additional question about Head Start. President Reagan, President Bush, yourself, I think all of us on this committee agree that it's a program that works. However, let me ask you the same question Mr. Obey asked you about the formal evaluation of another program.

Is the Department conducting a formal evaluation of Head Start in light of this effort to expand it?

Secretary SULLIVAN. Yes. There have been a number of evaluations through the years, and we are certainly continuing that effort.

Of course, one of the things that we have noted also is that this is the 25th anniversary of that program.

Mr. HOYER. I understand that there have been ongoing evaluations. But as you plan to expand the program to include all eligible three, four and five year olds that actually brings that percentage of 60 plus percent substantially down from where we are now.

You indicate $500 million would reach that objective. I would like to discuss that further at some point in time. I frankly think that is not enough.

Do we have, right now, any plans to have a formal full evaluation of how well Head Start operates, what seems to work better, and what seems to not work quite as well.

Secretary SULLIVAN. I need to talk with the directors of that program, but I believe that we do. I will get a response back to you in writing on that.

[The information follows:]

HEAD START EVALUATION

The Office of Human Development Services, Administration for Children, Youth and Families, recently awarded a contract to develop evaluation options for Head Start. This preliminary contract, using an expert advisory panel, will put emphasis on defining the variables that contribute to Head Start's performance and identifying those which maximize success. The report will be ready in September, 1990. The Department will use the advisory panel's results to determine the direction and design of subsequent Head Start evaluation projects, both short-term and long-term. The evaluation results will be used to encourage all Head Start programs to implement successful practices and approaches, to phase out less successful ones, and thus contribute to the overall improvement of the program nationally.

In addition, the Head Start program has an ongoing evaluation component through which projects are conducted to examine the effectiveness of individual service components, investigate the impact of the program on the children and families served, evaluate the feasibility and effectiveness of new experimental projects, and assess the value of certain programs and activities. Specific projects include determining what factors are more important than others in predicting positive outcomes for the child and family; evaluate what problems currently exist in the tran-

sition of children from Head Start to public school; and evaluations of how Head Start can better prepare parents to assume a greater role in their child's education.

CHILD HEALTH AND RELATED SERVICES

Mr. HOYER. Let me ask you about the child health, and related services. You indicate that there's been an expansion. In my community, and in communities across America, we have a critical problem with babies, either as a result of legal substance or illegal substance abuse by their mothers, placing an incredible burden on the health care, foster care and the school systems.

It's a time bomb waiting to explode in five years in our school system. Are we making adequate efforts to assist local communities in dealing with this problem from your perspective?

Secretary SULLIVAN. We have a number of things underway. None of us are really very happy about the phenomenon that we see with the Crack babies.

First of all, as you know, the President requested last year an expansion in the level of Medicaid eligibility to 130 percent of the poverty level and, of course, you and your colleagues in the Congress did respond and brought it to 133 percent of the poverty level for pregnant women and children. That helps.

The other thing that we are doing is looking at expanding funds for foster care, to help in the placement of children. We even have a small demonstration project in our Office of Human Development Services of $6 million to work specifically with finding better ways to afford placement of boarder babies and Crack babies.

But overall, funding for maternal and child health efforts amounts to about $3.5 billion. This includes dollars from various parts of my Department which are focussed on the problem of Crack babies.

Our infant mortality initiative, for example, which increases by a total of $63 million of targeted monies for outreach to pregnant women, including women who are taking drugs, is designed to help us with that.

I really think it's too soon for us to really say comfortably to you that we are doing everything we can, because clearly, we have a problem that we are still trying to understand the dimensions, not only in the number of babies, but also the long-term effects of drug abuse.

So, this is something we are monitoring, and we may very well be coming back seeking your help as we get more data as to the need for other initiatives.

CHILD SUPPORT ENFORCEMENT

Mr. HOYER. Mr. Secretary, because my time is limited, one more question.

You indicated that the infant mortality rate in our country was disgraceful. I think that is an appropriate adjective to apply to this phenomenon in the richest nation on the face of the earth.

In addition, another phenomenon that I think is disgraceful is that we have less than 50 percent of parents who are not living with their children.

Less than 50 percent are paying child support. I am going to get into this more deeply with the family support services people.

Do you believe, Mr. Secretary, and if you don't know at this point in time, I would like you to look into it, that it would be useful to have a Federal law making it a Federal crime to abscond from one state to another to avoid child support payments?

Secretary SULLIVAN. I will need to review this with my staff and get a response back to you.

We certainly are very interested in expanding efforts for child support enforcement. We have seen, I think, some significant increases in dollars for child support as a result of our efforts, though we are concerned as you are that we still are falling far short of what we should be doing, because obviously that means those children are either not getting appropriate financial support, or it means that the taxpayers are picking up the responsibilities of individual parents. In many instances, the parents have the capability of paying, but they have not met their parental responsibilities.

So we are certainly interested in finding ways to improve our child support enforcement activities. Whether a Federal law or some other activity is most appropriate is a matter requiring further review. I will get back to you in writing on that.

[The information follows:]

CHILD SUPPORT ENFORCEMENT

At this time, we do not have the information to determine if it would be useful to have a law which would make it a Federal crime to move from one State to another to avoid making child support payments. However, child support historically has been an issue for the State courts.

Currently, there are already actions underway which offer solutions to the problem of parents moving to other States to avoid having to pay child support. For example, regulations were recently published which established tough performance standards. Due to these regulations, States will be required to process interstate cases within specific timeframes. This requirement should result in States giving greater priority to enforcement of interstate cases. Second, the Office of Child Support Enforcement has levied audit penalties against States which have failed to fully implement provisions passed in 1984. These provisions can strengthen collection efforts, and include mandatory wage withholding, use of liens and bonds, and use of consumer credit agencies to enforce both in-State and interstate support orders. Third, HHS is developing an interstate telecommunications network which will facilitate communications between States in interstate cases through the electronic exchange of data.

Finally, the recently enacted Family Support Act of 1988 provided for the establishment of a Commission on Interstate Child Support. This Commission, which is in the process of being established, will be responsible for studying problems of interstate support enforcement and for making recommendations.

Mr. HOYER. Mr. Secretary, I would be interested in discussing that with you and pursuing it further. I am convinced that child support enforcement certainly is a related problem because one, two and three year old children in our country are receiving an inadequate education, healthcare, and a sense of personal worth. This country is going to pay a lot in the very near future for our failures in this step.

Thank you, Mr. Chairman.

HEAD START

Mr. NATCHER. Mr. Secretary, as Mr. Hoyer has pointed out, the Head Start program of course has to be reauthorized during the calendar year of 1990. At the time we marked this bill up, we

placed in the bill, $400 million as you know for Head Start. We carried it to the maximum authorized at that time.

Later on, after the completion of the appropriation bill, I believe the authorization was carried up to $1,550 million.

REDUCTION

Mr. Secretary, in your budget generally, as you know, as far as energy assistance, community services, and health professions, you are $1.5 billion under the 1990 level in President's proposal.

Mr. Secretary, don't you worry about it. We will take care of them for you, Mr. Secretary.

Now, generally speaking as far as Head Start is concerned, in the future, 1992, 1993, do you believe that we will have additional amounts requested over and above the amount that is now pending before the committee for Head Start? Are we traveling in that direction?

And I say to you, I think it is the right direction. How do you feel about it, Mr. Secretary?

Secretary SULLIVAN. Yes, Mr. Chairman. That is the direction that we are traveling. As you know, the President himself is committed to expanding the Head Start program until we have all eligible four year olds into Head Start or Head Start like experiences. We clearly aren't there yet, even with the proposed $500 million addition.

We expect to be back here next year, requesting additional funds beyond this. I think while we are pleased with what the President has agreed to for this year's budget, we clearly still have some way to go. The President knows that, so we expect to be asking for more support next year.

NIH GRANTS

Mr. NATCHER. Mr. Secretary, if you would just briefly now review for the committee the change in the last several years in regard to grants at NIH, the average size of grants, the average length of these awards, and when you get the transcript back, you can amplify it.

Just generally speaking now, what about the change in the last several years?

Secretary SULLIVAN. Yes. We have had a number of things happening with our grants out at NIH as you know. A number of years ago, there was a general agreement to try to keep the number of new research grant awards every year at the level of at least 5,000. This level has been generally achieved except for, I believe, last year, when we fell a little below that, to around 4,600 new and competing awards.

But the proposal that we have submitted in the 1991 budget would allow us to fund, I believe, almost 5,100 grants, or about 500 more than we are funding this year.

What has happened over the years is that the cost of research has escalated causing the average research grant award to increase. I think our average research grant award is now about $208,000 per award.

So research is much more expensive, and of course that is not surprising. As a result of the fact that the cost of research has risen more rapidly than our total budget, although our budget has indeed risen every year, we are facing a situation where the number of approved grant applications that are funded has decreased so that we are only funding around 25 percent of the approved grant applications.

That means that three out of four of the applications our scientific peer review groups say are meritorious and should be supported, do not receive funds through these grant programs.

That clearly has been a concern, not only because we are losing opportunities, but we are also concerned about what message this sends back to young people with innovative research proposals about the kinds of competition that they would be facing in seeking funding for their research.

We are pleased in some regards with what we have been able to do with NIH, but clearly we have a lot more meritorious work that we could do if we had the resources.

We have maintained the commitment to fund at least 5,000 new and competing awards in 1991.

Mr. NATCHER. Mr. Secretary, you have just about answered my next question, but since we read from time to time in scientific journals about the crisis in research funding as a result of the lower number of new grants, as a physician, a researcher, and past president of a medical college, what do you consider to be the current level of the biomedical research enterprise in this country, compared to five or ten years ago?

NIH SCIENTIST RETENTION

And I ask it again, Mr. Secretary, because we read these articles from time to time, how do you feel about it?

Secretary SULLIVAN. Yes, well, first of all, about ten years ago, we were funding, if my memory is correct, somewhere around, between 40 and 50 percent of the approved awards, so we really have dropped down significantly there. In addition to that, I think an equally troubling concern that we and others in the biomedical research community have relates to the training of new research personnel; i.e., the researchers of tomorrow.

One of the problems we have been concerned about on the campus of NIH, is that we have not been able to recruit a new senior scientist to the NIH over the past 10 years. This is for a variety of reasons, one of them being the salary structure that we talked about earlier.

Another interesting fact that I was not aware of until a couple of months ago is that of the visiting scientists who spend time on the NIH campus, about one-third are foreign nationals. This means we are training our scientific competition to a significant degree.

Given our significant research needs, Dr. Bromley, our White House science advisor, Admiral Watkins, our Energy Secretary and others, such as Admiral Truly at NASA, all are very concerned about the future research personnel of this country. Clearly we need to take a hard look at that and see what we can do to train more scientific personnel.

I guess the short answer to your question is I am concerned about the future of NIH, even though I think we have some excellent scientists there. They have stayed there in spite of the fact that they could earn three, four, five times as much if they were to go elsewhere, and they are always being recruited by universities and private industry. So we certainly need to be concerned about that.

Finally, we have an ad hoc committee that I put together of leading individuals from the private sector to work with us to take a look at the directorship of NIH to find out ways we can make that more attractive.

When that Committee finishes its deliberations later this year, I am sure we will be sharing that with you and seeking your help in addressing this.

BIOMEDICAL RESEARCH FACILITY REPAIR

Mr. NATCHER. As you know, Mr. Secretary, both Congress and your department have conducted a series of studies about the need for Federal support to repair and replace biomedical research facilities insofar as colleges are concerned.

From time to time on our committee, we have appropriated, your department has approved, small amounts to assist the colleges now to rebuild their facilities.

What is the Department's current position as to the Federal role in construction of extramural facilities, Dr. Sullivan? Just generally speaking.

Secretary SULLIVAN. This is one of those areas in which we really haven't been able to do what we would like to do because of the budget stringencies related to our budget deficit.

The surveys have shown that there is significant need for improvement of the research facilities of our universities around the Nation, because like our own NIH facilities, many of them are aged, and the equipment needs to be updated.

We haven't been able to mount that vigorous effort because of what we consider to be higher priorities at this juncture. These include carrying forward with the research grants themselves, and certainly the training of additional research personnel.

Hopefully, as our National deficit situation improves, we will be able to come forward in the future with some proposed solutions to the facilities problem.

Mr. NATCHER. Last year, Mr. Secretary, as you know, Congress appropriated $15 million for construction grants to be awarded competitively. What decision have you made now about the use of this money?

Secretary SULLIVAN. That process is underway. I have met with Dr. Raub, our Acting Director of NIH, and I know that between now and September 30th, those dollars will be awarded, even though the specific decisions have not yet been made.

I believe part of those monies will probably be going to support cancer research facilities.

Another concern has been to help replace the facilities of the Jackson Memorial Laboratories in Bar Harbor, Maine, a very unique research facility that supplies research animals of known

genetic strain to our research laboratories around the country. We expect that they will be applying for some of those dollars.

There will be applications coming from elsewhere, and we know that we will be unable to fund all the applications from the various institutions.

Mr. NATCHER. Mr. Secretary, as you know, on our subcommittee, we don't earmark a lot of these projects. In fact, we don't earmark any of them. You have thousands and thousands of them, but you have just expressed the opinion of our committee in regard to the $15 million.

In the conference, we said to the other side, we don't earmark these projects. We understand the need and the necessity for this $15 million.

Mr. Secretary, you have just spoken for the committee, and I want you to know it.

Mr. Conte, I am going to yield to you for five minutes, with your permission, and we will proceed.

I know the Secretary has a luncheon engagement, and we will then recess until 2:00 o'clock, Mr. Secretary.

Secretary SULLIVAN. Fine. Thank you.

Mr. NATCHER. Mr. Conte, I yield to you.

NIH RECRUITMENT AND RETENTION

Mr. CONTE. On the Head Start, Mr. Secretary, I want you to know that I filed a bill to bring up that $500 million to the Head Start, and try to get it authorized before we can mark up, maybe you could help, Steny, and if you can do that, then we can appropriate it in this committee.

Otherwise, the Chairman has a hard and fast rule that he doesn't appropriate unless it is authorized. On the salary thing, you remember last year I asked a lot of questions on that, and I am very concerned about not only not having a director, but the scientists that we have lost.

I think Lombardi Cancer Center over in Georgetown stole maybe 20 of them. Was it about 20?

Secretary SULLIVAN. I think between 15 and 20, yes, right.

Mr. CONTE. All in one fell swoop because of that.

Last year, I promised you that I would submit a bill creating a Senior Biomedical Research Service. I followed through, and I have introduced my bill which is to provide higher pay and benefits for top researchers at NIH.

It would make biomedical research far more attractive, especially for the young and talented investigators, and I hope that we can have some action to that bill this year, and we are looking for as many cosponsors on that as we can get.

What is the current situation with recruitment and retention at the institutes? In your professional judgment, do you still foresee a need, and I am sure you do?

Secretary SULLIVAN. No question about it.

Mr. CONTE. Better compensation for physicians and researchers.

Secretary SULLIVAN. There is no question about that, Mr. Conte. I visited the NIH campus in March of last year shortly after my confirmation and talked with some of the scientists there, and gave

them a chance to raise issues and questions with me. This was one of the first issues that was addressed to me and addressed most urgently because of the reasons you have already mentioned.

We have had discussions with our Office of Personnel Administration, as well as with other Cabinet Secretaries, because they have similar problems. Of course the Department of Energy with its own national laboratories, has difficulties with recruitment, the Veterans Administration with its Veterans Hospitals and their laboratories has a similar need, as does Admiral Truly with NASA.

So clearly, we have an urgent problem, and it's a problem that I think requires action as soon as possible because as I mentioned to Mr. Natcher a few minutes ago, we are in danger of eroding what I call a crown jewel for HHS, and that is NIH. The differential of three to four times salary is one that many scientists simply cannot afford. If they were considering only themselves, they might be able to do that.

But when they have children to go to college and other family responsibilities, I think that we are asking a great deal of them to forgo providing for their families in the same manner as their colleagues in the private sector.

We do need some help, and I am pleased to learn about your bill. We want to look at it and work with you.

Mr. CONTE. We will do all we can. Certainly as you may know, we passed a pay increase for all Federal employees, including Congress last year, and there is a move now on foot to repeal that. That would be devastating, I would imagine, to your department and to National Institutes of Health, would it not, if we were to repeal that?

Secretary SULLIVAN. Oh, no question about it. In our discussions thus far with possible candidates for the NIH Directorship, this has been a problem with a number of them. This is the most important biomedical research position in the world, and we shouldn't be having difficulties recruiting for it.

This is a position that people should want to undertake, and we do have a lot of people who are interested but simply cannot afford to accept because of the vast difference in the pay scale compared to what they are already earning, or what they could earn in the private sector.

So indeed, it's a significant problem.

Mr. CONTE. It's 11:30, so I will yield until 2:00 o'clock.

AIDS

Mr. NATCHER. Mr. Secretary, as you well know, as far as AIDS is concerned, back in the year 1984 we had $61.46 million in our bill, and we have come from that point down to 1990 $1,535 million.

And I believe the request at the present time before the committee is for $1,695 million; one of the most serious health problems before our country and around the world, you would agree with that, Mr. Secretary?

Secretary SULLIVAN. Oh, absolutely.

Mr. NATCHER. No question about it, and it's a matter that is of great concern to our committee, not only the amount of it but how it is spent. Help us solve this problem.

Mr. Secretary, thank you very much.
The committee will now recess until 2:00 o'clock.
Secretary SULLIVAN. Thank you, Mr. Chairman.

AFTERNOON SESSION

NIH FACILITIES

Mr. NATCHER. Now, Mr. Secretary, our committee is also concerned, as you know, about facilities on the NIH campus in Bethesda.

We have been told that the 1991 request is the beginning of a major effort to repair buildings built in 1950s.

We hear estimates of total cost of $800 million to $1 billion.

What can you tell us, Mr. Secretary, at this time about both your 1991 request and long-term needs in this area, as far as renovation and repairs are concerned at NIH?

Secretary SULLIVAN. Yes, Mr. Chairman.

Of course, our 1991 request is the beginning of that effort.

I believe we had some dollars in our budget for last year as well, but what we have on the NIH campus, as you have noted, are buildings that were built back in the fifties. They have long since been obsolete, and there is much equipment in those buildings that needs to be updated.

Our scientists at the National Institutes of Health, really our Nation's premier biomedical research facility, are not always operating with state-of-the-art facilities and equipment, and they should be. NIH is the center that all of the biomedical research community around the Nation looks to for leadership in research.

Our animal facilities, for example, really need to be upgraded so that they will meet all of the inspection criteria for housing those animals.

Our laboratories are crowded, and need a number of renovations.

Knowing that it is a significant dollar sum, and the budgetary constraints that we face, we anticipate phasing these renovations over several years. We will try to get all the resources needed to bring the NIH facilities up to date.

Mr. NATCHER. Dr. Sullivan, can you give us any idea, just a ballpark figure, as to approximately how much are we talking about by way of repairs over the next few years and all?

Secretary SULLIVAN. I will get back to you with the precise figure after consulting with our Acting Director on the NIH budget.

The figure that you mentioned of around $800 million would not be at all surprising. As you know, we have a number of buildings on the campus, including our clinical center, where our patients who are undergoing research treatments are housed.

So, indeed, that number sounds reasonable, but I will get back to you with a precise dollar sum once I consult with Dr. Raub.

[The information follows:]

NATIONAL INSTITUTES OF HEALTH INFRASTRUCTURE

Under current plans, the National Institutes of Health (NIH) estimates the cost of continued rebuilding of the Bethesda Campus to be approximately $700 million to $1.1 billion. This amount includes approximately $150 million for the campus infrastructure renovation program, $65 million to rehabilitate the older laboratory facili-

ties, $45 million for renovation of existing animal facilities, and $40 million for the Clinical Center safety and improvement project. NIH has not yet completed engineering studies for further modernization of the Clinical Center infrastructure. Preliminary cost estimates for such upgrades range from $400 million to $800 million, and account for the range of estimates for the total cost of rebuilding the Bethesda campus. It is anticipated that these projects will be phased in over the next ten years.

Additionally, approximately $300 million will be needed to complete the child health and neurosciences center, the consolidated office building, and AIDS facilities, as well as replace NIEHS laboratory facilities in Research Triangle Park, North Carolina.

INTERNATIONAL SUPPORT FOR RESEARCH

Mr. NATCHER. One other question, Mr. Secretary, concerning NIH.

Dr. Watson, whom you appointed to run the Genome Project has been quoted as saying that other countries are not paying their share of the cost of the basic research being conducted at the various institutes.

Are any steps being taken at this time to have Japan, West Germany, or any of the other countries support NIH directly?

Secretary SULLIVAN. Mr. Chairman, I know that Dr. Watson has had discussions with the scientists in those other countries about them paying their fair share to support the Genome Project specifically. He has noted—and I certainly agree—that this is a project that is going to be beneficial for all of mankind, and with our policy of open publication of our scientific findings, all Nations will benefit.

It has been striking that, over the years, a number of other countries have taken many of the discoveries that have come out of our laboratories, either on the NIH campus or in university laboratories supported by NIH funds, and have actually capitalized on those much to our financial disadvantage.

I believe that what Dr. Watson was referring to is the phenomena that all of us in the biomedical research community are increasingly concerned about, and that is having other Nations benefit, both in terms of improved health of their citizens, as well as the commercialization of our discoveries, without contributing financially. We feel that those nations should support the basic research that contributes to those commercial new products.

There are some discussions underway, and again, what I would like to do is consult with Dr. Watson and give you more precise answers as to just where we are in those discussions.

[The information follows:]

INTERNATIONAL SUPPORT FOR THE HUMAN GENOME PROJECT

To date NIH has not entered into any formal agreements with foreign countries to obtain their support for the Human Genome Initiative. A number of countries have already begun to sponsor research on the human genome including the United Kingdom, Italy, and the Soviet Union. We expect that in the near future France, the Commission of the European Community, and Japan will also establish national reserach efforts as well.

To encourage foreign countries to contribute financially to the genome project, NIH and the Department of Energy (DOE) have agreed to fund joint research projects between the U.S. and other countries if there is also financial support for the project from the other country. Neither NIH nor DOE will fund a foreign genome research project unilaterally unless the project will make a unique contribution to the initiative which can not be duplicated in the U.S.

In addition, a number of informal efforts have been undertaken to encourage international collaboration and participation in the effort to complete the mapping and sequencing of the human genome. Many of these informal efforts have evolved through the international scientific community. One such organization is the Human Genome Organization (HUGO). The President of HUGO is a representative of the United Kingdom, while representatives from the United States, Soviet Union, and Japan serve as Vice Presidents.

AIDS RESEARCH

Mr. NATCHER. This morning, Mr. Secretary, we mentioned and discussed somewhat in detail AIDS research, the cost beginning back in 1982 and up to and including the 1990 budget.

There have been a number of new developments affecting the AIDS epidemic and treatments from victims of AIDS.

Tell us now, Mr. Secretary, just briefly what changes you see in this area over the next three or four years.

Secretary SULLIVAN. Yes, Mr. Chairman.

First of all, I think we have made remarkable progress in our understanding of the AIDS virus from our research efforts and our scientists on the NIH campus have really played a leading role in that regard.

Of course, Dr. Anthony Fauci, Director of the National Institute for Allergy and Infectious Disease is our overall AIDS coordinator, so he has the administrative leadership role as well as the research that is coming out of the laboratories that he is supervising.

We understand a lot more about how the immune system works. Basically, the virus invades and attacks a certain class of lymphocytes in the body, the T lymphocytes which are responsible for the immune response that protects all of us from a variety of organisms. What happens as these cells are destroyed, and the immune system then becomes compromised, is the AIDS victim becomes susceptible to a number of infections from not only bacteria, but fungi, which normally would not represent a threat to anyone.

We have a great improvement in our understanding about how the immune system works, and have also gained insight into one possible way to approach the treatment of this disorder, and the prevention of the disease from spreading.

We know, for example, that there is a certain way the virus bonds to the cell surface of the T lymphocyte, and our scientists have been able to actually characterize that structure on the cell surface. They have been able to produce a replica of that protein. One of the therapeutic approaches involves giving the patient this replica of the protein.

By doing that, binding to the virus, it prevents the virus from binding to the cell and, thus, entering the cell.

Another of our outstanding scientists at NIH who has been actively involved, of course, is Dr. Robert Gallow. I am sure he is known to members of this committee, because he is the one who helped isolate and characterize the structure of the virus.

His work, of course, has been outstanding, and he has developed in his laboratory, along with a French scientist at the Pasteur Institute, a test kit for the diagnosis for the presence of the AIDS virus. The foundation has been established to utilize the royalties from that discovery to support the work of NIH in this field.

Diagnostic care has come from the work at NIH as well.

A third line of research has been the development of new chemical agents to try and attack the virus. Dr. Samuel Broder, the head of the Cancer Institute, suggested evaluation of a group of compounds synthesized back in the sixties by scientists at Burroughs Wellcome, in their attempts to find drugs to treat leukemia. Among the compounds they synthesized was Pseudothiamine, which ultimately, was not used for treatment of leukemia, because they found better drugs for that purpose.

As we learned about the AIDS virus, Dr. Broder suggested that we ought to explore these compounds to see if they would have an effect, and indeed, that is where our use of AZT came from. From that suggestion by Dr. Broder, the scientist at Burroughs Wellcome did carry out those tests.

Several things happened this year as a result of that.

About five months ago, I was pleased to announce the fact that not only individuals who have AIDS are helped by AZT or Zidovudine, but also that individuals who have the virus, but who have not yet developed symptoms of the disease, are helped by AZT. AZT also prolonged the period before they became symptomatic from the virus.

The final announcement we were able to make was that the use of AZT in children also was effective and that the incidence of complications from AZT was no greater in children than in adults.

The FDA has now approved the use of AZT in children with AIDS, which gives us a significant advantage.

Another thing that is very promising is dideoxinosine, or DDI, a drug that was produced by Bristol-Myers. That drug, as you know, Mr. Chairman, is in the trial period. Bristol-Myers has made the drug available free of charge to individuals with AIDS who do not qualify for some of the clinical trials that are underway for AZT.

Some patients can't take AZT because it is too toxic. They may get anemia, or have other symptoms.

These patients may be helped by dideoxinosine.

The final research development which I think over the long haul has great promise, is the development of a vaccine against the AIDS virus.

I can't predict just when we would be successful with that, but our scientists at NIH have indicated their optimism that with which we will be able to develop such a vaccine with which we could immunize our population, and perhaps prevent infection from this virus.

There is a lot of work underway, and over the last seven or eight years, I think the rate of discovery and growth of our knowledge about the AIDS virus, treatment, and development of therapies has been remarkable. Our scientists at NIH have been right in the leadership of these efforts.

AIDS BUDGET

Mr. NATCHER. The requested amount for AIDS, as you well know, in your budget, is $1.695 million.

Mr. Secretary, did the Department request substantially more than this amount from the Office of Management and Budget?

Secretary SULLIVAN. Mr. Chairman, I would have to go back and look at my notes. I know that our Public Health Service, as they developed their initial budget drafts, did have a higher request. I believe, that they wanted to have something like $2 billion or $2.1 billion for that effort.

In the Department as we put together the budget request from our various components, because of the various competing needs, we did not recommend the full amount that they asked for.

Our request of OMB, Mr. Chairman, was for $1,760 million, so that we got almost the amount that we asked for, but not quite.

PEDIATRIC AIDS

Mr. NATCHER. How much is included in your budget for various programs directed at pediatric AIDS patients in 1991 and how does this compare to spending on this problem in 1989 and 1990, Dr. Sullivan?

Within the last week, a lovely little lady came to visit with me, very much concerned about this matter.

She was on 60 Minutes; you may have seen her.

She will be back to testify before our subcommittee as an outside witness, and we are very much concerned about this matter.

Tell us what is happening now as far as pediatric AIDS patients are concerned, Dr. Sullivan.

Secretary SULLIVAN. Yes, Mr. Chairman.

Our budget request for pediatric AIDS, as I recall, is something like a 25 percent increase over 1990. In 1987, our budget for pediatric AIDS was about $19.5 million and then for 1988, it jumped considerably to almost $71 million.

For 1989, it was $98 million, for 1990, it was almost $137 million, and for this year, our request is almost $172 million.

So it has gone from $19 million in 1987 to a request this year of almost $172 million.

Mr. NATCHER. At this time, Mr. Secretary, I yield to Mr. Young of Florida, one of the good members of this committee, and a gentleman that has always been concerned about health and education, and every time we take our bill to the Floor, he is right there with us, Mr. Secretary.

I yield to him at this time.

BONE MARROW DONOR REGISTRY

Mr. YOUNG. Mr. Chairman, thank you very much and please forgive me, Mr. Secretary, for missing the morning session, which I spent with the Secretary of Defense and the Chairman of the Joint Chiefs, General Powell. But it is nice to be with you this afternoon, and you have my welcome to the committee.

I know you have already been warmly welcomed by my colleagues.

Mr. Secretary, one of the most rewarding experiences of my whole life has been working for the establishment of the National Bone Marrow Registry. As you know, early on the agency that you now head was less than enthusiastic about the program, and actually preferred not even to have any responsibility for it. So some years ago, we established this registry through the United States

Navy, with funding from the defense appropriations bill rather than from this appropriations bill.

Since then, the success of the program has been great and lives are being saved, as you well know.

A lot of enthusiasm has been created here in the Congress and throughout the media, and today NIH is the agency that has jurisdiction for the program, and administers the program.

It is going along very well and the news is good.

In the last two years, we have done about 250 transplants using the registry, with about a 70 percent success rate on patients who were terminal without this procedure.

Our problem is—and it is being highlighted right here in Washington, D.C. today—our problem is that we still don't have enough names of possible donors in the registry.

We have about 70,000 names now. We would like to have about 100,000 names in the registry by the end of the year, and hopefully eventually we will have at least 250,000 names.

The reason we need some names and some possible donors is the fact that the typing of the marrow has to be so exact that you can't just willy-nilly take bone marrow from a donor and give it to a recipient without all of the necessary matching.

Now, I am looking for advice. We are going to try a pilot program in my district to encourage people to become donors, to be typed, to have their bone marrow typed so they can go into the registry.

Here in Washington, D.C., we have two cases right now, two young ladies who are in dire need of a bone marrow transplant and who can't find a donor.

The list of names in the registry just is not adequate today.

We are hoping that we can find some way to get the message throughout the United States and, as a matter of fact, we are working internationally with other friendly nations now to establish an international registry, and we are hoping that you might have some ideas how we can, in fact, get more possible donors into the registry.

I have talked with White House officials and I have communicated to the President and he hasn't responded yet about the possibility of advising those in the military services about this program to see if they would be willing to have their bone marrow typed.

Typing bone marrow is no problem for the donor, because you draw the blood the same as if they were simply typing the blood.

The problem is that there is a $75 fee per person typed and that gets to be somewhat expensive.

So we are looking for some ideas.

I think this committee and this Congress is willing to continue to appropriate and support the registry.

It is saving lives; it is dramatic in the way that it is saving lives.

What advice can you give us on how we might get this message out to encourage more people willing to become potential donors and have their bone marrow typed?

BONE MARROW REGISTRY

Secretary SULLIVAN. Thank you very much, Mr. Young.

Let me say this: First of all, as you may know, my professional background is in Hematology, so I am intimately familiar with the problems and the issues here. In fact, the plight of these two individuals here in the Washington area has been brought to my attention, because our laboratory at the Heart, Lung, and Blood Institute, has been active in helping them with some of the testing and typing that has been done.

These two situations highlight one of the critical problems because, as you point out, contrary to other kinds of organ donations, the typing for bone marrow has to be so much more precise, in terms of the marrow graft-taking. It requires, therefore, a large pool of donors to try and get the best possible match.

Otherwise, the bone marrow graft, doesn't take.

The Registry that you alluded to is being operated by our Blood Division at the Heart, Lung, and Blood Institute, and their function is indeed to maintain the data as to those typings and where the individuals are, so that the matches can be done.

The funds that we have, which are around $4 million for the operation of this facility, are for administrative costs, for the personnel and the computers, et cetera.

One of the problems that we are confronting right now is that a number of families don't have the funds to pay the cost for the typing. Since you might have to go through several hundred or even several thousand people before finding a suitable donor, at $75 per test, the process can be extraordinarily expensive, and prohibitive, even for reasonably affluent families.

That represents a real problem which we cannot answer at the moment. We have a task force in our Department looking at this question.

The other problem that these two situations presents is the fact that both of these individuals are members of minority groups.

One individual—and both of them, I believe, have leukemia. One young lady is Jewish and the other is black.

The fact is that the likelihood of getting a compatible bone marrow graft is greatly reduced for members of certain ethnic groups. In terms of our major blood groups used for ordinary blood transfusions, there is no problem.

Those groups are shared by the entire population—white, black, Asian, or what have you. But when it comes to a marrow graft, you then are looking at a whole lot of what we call minor antigens, antigens that can cause rejection ultimately with the graft.

What these two cases have highlighted—and there are other cases around the country—is the need to get more members of minority groups registered as possible donors, because in the case of minority groups, we have not, for a variety of reasons, been successful in getting a significant number registered.

For the lady who is Jewish, the effort to find a compatible donor even reaches as far as Israel.

About four weeks ago, I was in Israel visiting the Minister of Health of that country because we have some international health agreements with them. While I was there, I learned that there was an activity underway to try and find within the Jewish community in that country, a possible donor for that young lady.

We certainly want to do everything that we can in the Department to highlight this need, and to emphasize it and to invite individuals to come in for testing. I think the response in the case of both of those young ladies with their unfortunate situations has been that the community has rallied, but it really is a case where this is not widely known.

So we certainly intend to contribute in whatever way we can to emphasize the need for expanding that donor pool.

One final comment I would make, regarding this is that, unfortunately, while we have tremendous technological capabilities, once you find a donor, you have an expense of between $150,000 to $200,000, which is the cost of the marrow transplant itself, and that represents another financial problem.

Clearly, this is one of those instances where our increasing capability medically is also raising other strains, stresses, and questions in terms of our ability to pay for that technology.

BONE MARROW REGISTRY

Mr. YOUNG. I appreciate your response, Dr. Sullivan, and I would like to say that I am much aware of that, because in the beginning, I understand that none of the insurance companies would participate in the cost, and we have been working with them, trying to educate them to the dramatic results of this procedure.

We are finding out that some of the insurance companies are willing to be part of the effort.

It is such a great lifesaving procedure that it is too bad that we are running into these problems.

Let me ask just one more question. My time has probably already expired, but one of the approaches that we are using—we are meeting with the Executive Board of the Bone Marrow Registry in my district in a couple of weeks to kick off this pilot project, and one of the things that we are going to try to do is to get large employers to try to educate their employees to see if they would be willing to be typed, and have the employer contribute to the cost of the typing.

If that is successful, then we are going to ask maybe that we will try to do this on a nationwide basis.

But if they are willing to do that as private employers, suppose we went to Government agencies and asked the same thing.

Would you think that it would be valuable and/or appropriate that the Government would pay $75 for the typing cost of an employee of a Federal agency?

Secretary SULLIVAN. Well, that certainly is something that we would want to examine. I think there are a lot of questions as to what the net yield might be, but certainly we would be open to exploring that idea.

This is a problem that our scientists in this field are very concerned about and very active in. I can tell you I received correspondence from Dr. Richard Aster of the Milwaukee Regional Blood Center, one of the nation's outstanding regional blood banks for many, many years, who has been involved in the forefront of blood typing.

It indicated to me his involvement and his concern that we look further at opportunities to make advances.

Secondly, about three months ago, scientists at the University of Washington School of Medicine in Seattle asked me to help them make contact with scientists or physicians in Japan for a trip they were making there for scientific purposes. We were able to arrange an introduction for them with the officials in Japan, to try and develop a relationship there.

When it comes to our citizens of Japanese discent, clearly if we developed a number of individuals of Japanese origin for our registry, that could help as well.

It is a very significant problem, and one that we are reviewing to see what we can do.

Mr. YOUNG. Mr. Secretary, thank you very much. I would like to ask several more questions about the abandoned Infants Act, and I will submit those to you in writing in the interest of time.

Secretary SULLIVAN. Thank you.

Mr. YOUNG. Thank you, Mr. Chairman.

Mr. NATCHER. Mr. Smith, I now yield to you.

Mr. SMITH. A follow-up on that discussion that we had this morning.

How many names do you think should be in the registry?

BONE MARROW REGISTRY

Secretary SULLIVAN. Probably several million. I can't give you a precise number off hand, because the fact is, that you must consider the minor antigens and antigenic differences with each ethnic group. Ideally we would want to have not only blacks and Hispanics, but certainly Asians, Native Americans, and so on.

Mr. SMITH. Anyway, the goal would be several million?

Secretary SULLIVAN. Oh, yes. It would require that, because even within those groups, it takes a large number of individuals to make sure you have the compatible donor.

MEDICAL LIBRARY SYSTEM

Mr. SMITH. What could you tell us about the medical library situation? How adequate is it?

Secretary SULLIVAN. The national library of medicine, or the——

Mr. SMITH. No. I mean throughout the country. The availability of adequate medical library services?

Secretary SULLIVAN. To my knowledge, Mr. Smith, I think we are doing reasonably well there. This results not only from the efforts of our colleagues at the National Library of Medicine, who worked with our medical librarians around the country, but also from our efforts to develop and strengthen our academic medical centers over the past 30 years or so in this country.

There has been a significant emphasis on developing the capabilities of our libraries, not only with the holdings within the libraries themselves, but also the development of an active library network.

We actually have a network in this Country now where virtually every major medical library is connected with every other library. So that—for example, when I was at Morehouse, we were connect-

ed with a library network that was operated out of Columbus, Ohio, and they had all of our holdings there. Through that connection, if we had a call for a rare book that we didn't have, we could know within a minute or two where that book was.

It might be a library out in Chicago, or Los Angeles, and we could make a request for that book, and usually within a period of three or four days, we would have it.

Mr. SMITH. These library services are somewhat regionalized, is that right?

Secretary SULLIVAN. Yes, they are regionalized, but then, of course, the regions are connected to each other, so in effect we really have a national system.

Mr. SMITH. As for Iowa, it is really not as adequate as it could be. Are you acquainted with their problem?

Secretary SULLIVAN. No, I am not aware of that. But I certainly would be pleased to learn more about it. As you already know, you have an outstanding medical center in Iowa.

Mr. SMITH. We have two, the biggest medical education institution I guess in the country, the Osteopathic medical school, and then we have Iowa University.

Secretary SULLIVAN. Yes, I am familiar with them, and they really are outstanding institutions, as well as the Veterans' Hospital in Iowa City affiliated with the medical school there.

If they are saying that there are some problems with the library system, I am not aware of that. I would like to learn more about that.

Mr. SMITH. Do you need a different type of library for universities, for medical schools, than you do for the doctors or not?

MEDICAL LIBRARY SYSTEM

Secretary SULLIVAN. I guess there are perhaps some quantitative differences.

Basically, the libraries of our medical schools have tremendous capability, as I mentioned, because in addition to that kind of network, the libraries have all adopted the same cataloging system, which really means inventory is very easy among the libraries.

But we also have through our National Library of Medicine, what we call our Medline. If, for example, a doctor in Atlanta, whether he is at a medical school, or in practice, wants to find out what has been published on pediatrics, for example, in the last six months; he can make a request through our Medline, and, within a matter of perhaps 10 or 15 minutes, through the computer system, have a printout of the listings of all of the publications on that particular subject.

Mr. SMITH. Are regional library services usually at a university?

Secretary SULLIVAN. Yes. They are usually at a university, because you need to have a well-trained library staff to effectively operate that system. But they serve the entire community, hospitals, and physicians.

Mr. SMITH. Rural doctors and everybody else?

Secretary SULLIVAN. Oh, yes, very definitely.

For example, in Atlanta, the Calhoun Library at Emory Medical School was the regional library for that area. The next regional li-

brary, I think, was at the University of Alabama in Birmingham. They connected with virtually all of the hospitals and other facilities in that area. That has worked very well.

One of the things that is going on with our library system is that it is moving more towards computerization, not only of holdings, but also of articles. Our librarians would like to move more and more in that direction, because with publishing occurring at such a rapid rate, the standard library within a relatively short period of time, becomes filled to capacity. Many of our libraries have the capability of putting all of this on computer tapes, and are proposing that we move towards a computerized system of storage, retrieval, et cetera.

Mr. SMITH. Has that not been done?

Secretary SULLIVAN. No. Only in a few instances. I believe the Georgetown Medical Library is very advanced along that line. I am not sure if they have that completed. Such a conversion tends to be expensive, but once you have converted, the maintenance cost is not that great.

Mr. SMITH. Well, I won't take more time now, but I want to talk to you about this situation with regard to the Midwest.

Secretary SULLIVAN. Fine. I would be pleased to do so.

Mr. NATCHER. Mr. Conte, I yield to you at this time.

LONG-TERM CARE FOR SENIORS

Mr. CONTE. Thank you.

Doctor, with the repeal of Catastrophic Insurance last year, we are now back to square one in finding a decent solution to long-term medical care for our senior citizens. In fact, the problem seems to be getting worse every day.

Medi-Gap insurance rates have leaped all over the country after the repeal. Rates in Massachusetts are up 67 percent; it is just unbelievable. And our seniors are now paying a very heavy penalty for the loss of the catastrophic coverage.

What do you think ought to be done to provide seniors with adequate protection against a long-term illness?

Secretary SULLIVAN. Thank you, Mr. Conte.

I expressed great reservations about repealing the Catastrophic Legislation last year because I maintained then, and still maintain, that that Bill was one which provided real services needed by our citizens. I haven't seen anyone come forward to refute the position that I and a number of others have taken, which is that that repeal was really a very finely orchestrated effort of a relatively small number of individuals here, and regretfully, we now have this problem.

There are several things that we are reviewing, because, as you pointed out, the need is there, and we certainly want to find ways to address it.

The first is the fact that in our budget proposal for this year, we are emphasizing expanding our capability for managed care. This includes care provided through Health Maintenance Organizations (HMO) and Preferred Provider Organizations (PPO). In that context, one of the things we are proposing is a new program, Medicare Plus. This would be a program combining a HMO or PPO with

a Medi-Gap insuror. Another part of our managed care proposal is to reimburse risk-based HMOs at 100 percent of their average annual per capita cost.

We have been reimbursing them up until now at 95 percent of that cost, based upon the fee-for-service structure in the pertinent region.

Increasing the reimbursement rate to 100 percent will give added funds so that additional benefits and reduced costs can be provided either directly by the HMO or through a rebate to the subscribers.

In this way, we feel that we can not only provide comprehensive care with continuity of care, but also prevention services which managed care operations also offer. In addition, this provides a way to get a handle on cost escalation.

Those are two proposals that we hope that the Congress will approve.

Secondly, as you know, the President, in his State of the Union Address, asked me to lead an effort in the Domestic Policy Council to examine questions about the quality of the care that we are giving, the access to care for older citizens, and cost control. We will be looking at the kinds of provisions in the Catastrophic Bill of last year, along with other things, including such questions as how to approach the issue of our 31 million uninsured Americans.

We are very concerned about that, as well as the dimensions and needs for long-term care, and some of the strategies for providing that.

Last September, I appointed a Departmental task force to begin looking at these questions under the leadership of Constance Horner, our Undersecretary. We already have many of our staff looking into this.

In addition, of course, the Pepper Commission under Senator Rockefeller's leadership is looking at that, and we are looking forward to their recommendations.

Thirdly, the Quadrennial Advisory Council on Social Security and Medicare, appointed last summer and headed by Debra Steelman, will be reporting this summer on some of the questions regarding, and approaches to, long-term care as well.

That is just the beginning. We will also be looking to, and inviting from, the private sector, their analysis of the situation. We believe that we need to look comprehensively at the whole issue. The Catastrophic Bill, while certainly one that we supported and felt was needed, was looking only at a part of the issue.

We need to take a comprehensive look at the issue, and invite broad public discussion and debate. One of the problems that the Congress was faced with the Catastrophic Bill was that a lot of senior citizens really did not understand what the Congress had passed.

Whatever we do, we want to be sure that there is broad public discussion. If we do our job right, we are going to be issuing some options that, if they are adopted, will make significant changes in our system.

We don't want to go through a debacle like the one we went through this past year. Therefore, we think that this subject really needs broad discussion within Government, in the private sector, and with all of our citizens.

So we are looking forward to that.

PEDIATRIC KIDNEY DISEASE

Mr. CONTE. I am glad to hear that. I agree with you. I voted against repeal. It is really sad the way the senior citizens were stampeded by a few people, and they are paying for it now right through the nose, and a lot of them just can't afford it.

What can NIH do to improve research on pediatric kidney diseases?

Secretary SULLIVAN. To give you a good answer for that, I would like to consult with our colleagues at NIH and get an answer back to you. I know that I will be getting good advise from Dr. Antonia Novello, our nominee for Surgeon General who appears for confirmation tomorrow. Her special area of expertise is pediatric kidney disease. I will get a response back to you in writing.

[The information follows:]

PEDIATRIC KIDNEY DISEASE

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has primary responsibility within NIH for research on kidney and urologic diseases. These disorders affect an estimated 13 million Americans and, in the case of kidney diseases, can lead to irreversible renal failure, or end stage renal disease (ESRD).

The NIDDK research program is focused primarily on understanding the causes and mechanisms of various kidney diseases. Of those renal diseases leading to renal failure, nearly 70 percent have their onset during the pediatric age. These include the two major causes of ESRD, diabetes mellitus and hypertension. These diseases have an annual direct cost to the Federal Government in excess of $4.4 billion. This figure does not account for indirect medical and social costs.

There are two additional trends of note in this area. First, the number of new pediatric nephrology patients has increased by 11 percent over the past decade. Second, the renal failure among minority populations occurs at a rate that is between five and twenty times greater than the rates experienced ten years ago.

Children may also develop kidney diseases from a variety of genetic and non-genetic disorders. Among these ailments are Alport syndrome, juvenile nephronophthisis-medullary cystic disease complex, and polycystic kidney disease (PKD). PKD is inherited as an autosomal dominant disease. Like diabetes and hypertension, PKD reaches end-stage in adults but is present at birth and slowly develops during childhood. PKD represents five to ten percent of the overall ESRD population.

Knowledge gained from studies of adults with kidney diseases is often applicable to children as well. Many technical and therapeutic advances have allowed children with these diseases to survive and prosper. Nonetheless, there is still no standard treatment and progression of the disease can not be stopped. The search continues for a better understanding of kidney disease and for more permanent treatments. The most important conceptual shift now becoming obvious is that therapy must begin during the pediatric age.

We recognize the shortage of research personnel in pediatric nephrology, and consequently NIDDK currently supports nephrology research training programs at 28 U.S. medical schools. Three of these programs specialize in pediatric nephrology. NIDDK staff will continue to encourage increased grant applications in this field.

Mr. CONTE. The budget proposal has $24 million more for NIDDK, and I know you just said you would talk to your people, but is there enough money, do you think, to develop centers of excellent programs for pediatric nephrology?

Secretary SULLIVAN. If I might, Mr. Conte, what I would like to do is fold my answer to that in with the communication I will send to you, because I simply am not close enough to that particular question to really give you a meaningful answer today.

Mr. CONTE. And when they come up, we can develop it.

[The information follows:]

FUNDING FOR PEDIATRIC NEPHROLOGY

In 1991, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) will spend approximately $98 million to support basic and clinical studies on kidney diseases. Given the wide range of program responsibilities of the NIDDK, the 1991 budget plan does not call for development of a center of excellence in pediatric nephrology. Nonetheless, we will use the additional funds requested to intensify research and training efforts in this field.

TREATMENT OF SEIZURES WITH PHENOBARBITAL

Mr. CONTE. I want to know what we can do to improve research in this field. Today's Post article on children seizure drugs, it was something in the newspaper, I don't know if you saw it. It said there is a disturbing report out of NIH that phenobarbital, a widely used drug, given to control children's seizures may inhibit the development of the child's intellectual growth.

Can you shed more light on this report? Is there cause for concern here?

Secretary SULLIVAN. At this juncture, I would say that I would not want to suggest that there should be concern. This is something that we are going to be reviewing, because, quite frankly, I was surprised to see that report myself.

Phenobarbital is a barbiturate that has been around and used for the treatment of seizures for many years. It was widely used back in the 1950s when I was a medical student. I am surprised that if there is such an effect that we are only seeing reports on it now.

I haven't had the opportunity to see those data first hand. I want to reserve any further comment until we have a chance to examine the report, both the point that it may retard mental development, and that it may not be really effective for treating seizures. If that really is the case, there have been a number of very good neurologists who really have been misled.

That is something that I will review and on which I will be glad to report back to you.

[The information follows:]

PHENOBARBITAL AND SEIZURE TREATMENT

The results of the study on phenobarbital recounted by the Washington Post, were originally reported in the New England Journal of Medicine. This study was funded by the National Institute on Neurological Disorders and Stroke (NINDS) and focused only on the use of phenobarbital as a treatment for febrile seizures, seizures which occur in about 3 percent of children under age 6 when running a high fever. The study did not evaluate the use of phenobarbital as a treatment for seizures caused by other disorders such as epilepsy.

The study involved 217 children between the ages of 8 months and 36 months who had experienced a febrile seizure and were at risk of further such seizures. It concluded that using phenobarbital to treat febrile seizures was not effective in preventing the recurrence of those seizures. Further study will be necessary to obtain results on a more general scale.

SSI OUTREACH

Mr. CONTE. I have been working, Dr. Sullivan, with Gwen King, commissioner of SSA to start a new SSI outreach program, and she came to me early last year and told me that it was her top priority. This committee put $3 million into getting the SSI outreach program going.

The SSA just put out a request for ideas from communities in area agencies on aging, and outreach will seek out potentially eligible people, let them know what benefits are available to them. There was no money in the budget request to continue this program.

Do you foresee a continued need for SSI outreach activities?

Secretary SULLIVAN. Oh, very definitely. I will have to talk to Commissioner King because I know this is a very high priority of hers. She has sent letters to all of our Social Security staff and our offices around the country about the need for outreach and the need to be sure that all citizens who are eligible for programs administered by the Social Security Administration, receive those benefits. If there are cases where there is some question as to continued eligibility, a review must be carefully prepared before any reduction or discontinuance of benefits is made.

I know that Commissioner King has strong feelings about this, and that she has gone out into the field with some of our workers, into shelters for the homeless for example, to ensure that we are getting to all of the individuals who are eligible for benefits.

This is going to continue to be a priority of the Social Security Administration, and I am confident that there is money in that budget for outreach. I can assure you this effort is going to continue.

Mr. CONTE. My 10 minutes are up, but Mr. Chairman, I want to make one observation in closing.

Dr. Sullivan has really handled himself admirably here today. You and I sit here every day in and day out and other members of the committee, and I sit on a lot of committees as ranking Republican in appropriations.

You are one of the few I have ever seen come up here at the table all alone. Most of them come up with an army. And you have been up here all alone and you answered every question. You did a great job, too, Doctor.

Secretary SULLIVAN. Thank you, Mr. Conte. I appreciate that.

Mr. NATCHER. Mr. Stokes, I yield to you at this time.

BUDGET EFFECTS ON HEALTH CARE SYSTEM

Mr. STOKES. Thank you, Mr. Chairman.

Mr. Secretary, the President's budget calls for a $5.5 billion reduction in the Medicare budget. Hospitals, Representatives from hospitals in cities, such as Cleveland and other major cities in the country, are visiting with their representatives, and they are expressing the fear to us that this $3.5 billion reduction in part A of the Medicare budget is going to force reductions in services. The fear that it is going to force some of the hospitals to close.

I would just like to know what your comments are as to whether you think that the health care system can function within the level proposed by the President's budget without cutting back services and without the possibility of more hospital closings.

Secretary SULLIVAN. Well, let me see if I can give a clear and short answer to your question, Mr. Stokes. Yes, I think that they can, and let me tell you why.

First of all, we really are committed to reining in our cost escalation. Prior to 1983, our annual hospital inflation rate was running at 18 percent. Since the implementation of Diagnostic Related Groups (DRG), and the Prospective Payment System (PPS), we have brought those costs down significantly. They are now increasing at around nine or ten percent annually.

That is a significant decrease and we are very pleased with it, but we feel that further improvements can be made because medical cost inflation at our hospitals is still running about twice the consumer price index.

Hospitals in our inner cities have an occupancy rate of around 65 percent. Rural hospitals, by the way, are around 43 percent. What that means is we still have a lot of excess capacity. We are paying for capacity that we really don't need.

What we are trying to do is to bring those costs under control so that we can have dollars available for other medical and health needs such as expanded prevention services. Of course, we are concerned about such things as what the care of AIDS patients is going to cost a few years down the road, because we haven't seen the worst of that yet.

I am convinced that our colleagues in the hospitals can work with us, and that this budget will prove to be sufficient.

Our inner city hospitals frequently qualify for funds under our disproportionate share payments which go to hospitals serving a disproportionate share of lower income patients. Those hospitals also, because they are frequently teaching hospitals, have certain costs for their house staff funded through indirect medical education payments. They also receive additional medical education funds to pay the salaries of the resident staff.

Finally, this past year our recommended update in the reimbursement rate for both rural hospitals, and hospitals in large urban areas, was greater than that for other hospitals.

All of this was done, recognizing the fact that these hospitals have a greater intensity of sick patients and a higher percentage of bad debt. The adjustments that we have made to address this should be sufficient.

It certainly will require the cooperation and help of hospital administrators as we try to rein in costs, but I believe that our budget is adequate.

AIDS–AZT TREATMENT

Mr. STOKES. Let me go back to the AIDS problem, which you addressed a little while ago, and during the course of your reply, you made reference to AZT treatment and how effective it was. But the President's budget does not request funds to continue the AZT treatment grants, which were at $29 million in fiscal year 1990.

Considering the effectiveness of AZT treatment, which you have already articulated for us, tell us why no funds are requested for the HIV/AIDS treatment grant program.

Secretary SULLIVAN. There are several reasons, Mr. Stokes. First, we believe that because individuals who are eligible for Medicaid, as well as Medicare, have this drug paid for through those pro-

grams, that the Federal Government really is participating in providing this drug for those individuals.

Secondly, now that we have shown that this drug is effective, more and more insurance companies are covering AZT for those individuals who need it.

Thirdly, in the same way that I think this committee is rightly concerned about the propriety of earmarking funds here for specific things, we have a similar situation We don't believe it is appropriate to earmark funds for a specific drug, because were that to proliferate, within a relatively short time, we would have an administratively unmanageable system.

We believe that what we need for our health care system is the broadest possible flexibility. While this year we may have the demand and the need for AZT or other drugs for AIDS patients, five years from now, we may have a different profile of need. If we were to build into our system that kind of categorization, this would really add to the complexity of managing our health care system, and would lead to some inequities. Those individuals who are eligible for medical assistance are reimbursed, and we believe that to be appropriate means

PEDIATRIC AIDS

Mr. STOKES. Let me ask you about a couple of other programs in this same area. I know that no funds were requested for AIDS home health care and subacute care programs. At the same time, although we note that the number of pediatric AIDS cases is increasing at an alarming rate, your request in the budget is only $14.7 million for pediatric AIDS demonstration grants, which represents a decrease of about $68,000 from the fiscal year 1990 level.

I would like to know what percentage of the AIDS budget is targeted towards pediatric AIDS and whether this is really enough, given the added magnitude of this problem.

Secretary SULLIVAN. The total amount in our budget for pediatric AIDS is $171 million. Thus far, we have had approximately 115,000 patients diagnosed with AIDS in the United States since this disease was first recognized. The number of pediatric cases, that is age 13 and under, is not quite 2,000.

When we look at the number of those individuals with pediatric AIDS and the fact that we are spending $171 million, it seems that this is a very significant and appropriate increase in our overall pediatric AIDS budget from 1990 to 1991. We have given consideration to all of the competing priorities that we have for funding, and this 23 percent increase for pediatric AIDS is significant.

HBCU RESEARCH FACILITIES

Mr. STOKES. And in the amount of time I have left, let me ask a question about the human genome research project, which you have already referenced and for which a substantial amount of money has been requested. As former president of Morehouse School of Medicine, I know you are familiar with the research capability of our nation's historically black colleges and universities.

A DHHS report on extramural biomedical research facilities construction dated June 19, 1989 acknowledges that HBCU's are at a disadvantage in gaining access to facilities funds.

In general, do the HBCU's have the physical infrastructure to participate in the human genome project and other major science initiatives, and if not, I would be interested in knowing if you have a plan to increase the research capabilities of the HBCU's.

Secretary SULLIVAN. Mr. Stokes, I think we need to review that closely in terms of the genome project specifically. Certainly the genome project is a very significant one. When that program is fully developed, we anticipate an annual budget of around $200 million annually over the next 15 years. Clearly that is a significant effort.

The research infrastructure at our black colleges and our health professions schools is improving significantly through a number of measures. The minority institutions program which you initiated here has been working very well in terms of increasing the research capability in those institutions by providing the kinds of resources needed for research. On the genome project specifically, I will need to get back to you. I will be happy to look into that and get a response back to you.

[The information follows:]

HBCU PARTICIPATION IN HUMAN GENOME RESEARCH

Historically black colleges and universities (HBCUs) currently do not have the facilities or trained personnel to participate extensively in the human genome research program.

Genome research requires very sophisticated equipment and large groups of highly specialized scientists and technicians. Currently the program research is being conducted primarily at major research institutions and large biotechnology companies. Such institutions have the critical mass of people and research infrastructure necessary to move the project forward at an optimal rate.

We recognize that inadequate research infrastructure places HBCUs at a disadvantage in competing for funds for projects such as the human genome initiative. We are trying to address this historical problem through several programs. The Research Centers at Minority Institutions (RCMI) program is specifically designed to assist HBCUs develop their research infrastructure. The Minority Access to Research Careers (MARC) program and the Minority Biomedical Research Suport (MBRS) program actively promote the participation of minorities in biomedical research careers.

Recongnizing the potential profound effect of human genome research on health care, the National Center for Human Genome Research (NCHGR) is very interested in exploring ways all biomedical research institutions, particularly HBCUs, can participate in, and contribute to, the human genome project. The RCMI program is one possible mechanism. We are evaluating currently how NCHGR can participate most productively in the RCMI program.

Mr. STOKES. Thank you very much, Mr. Secretary. Thank you, Mr. Chairman.

AGENCY FOR HEALTH CARE POLICY AND RESEARCH

Mr. NATCHER. Last year's reconciliation act, Mr. Secretary, as you know, created a new agency in the public health service known as the Agency for Health Care Policy and Research. Can you tell us generally what the mission of this agency is, and how will it be organized into your Department?

Secretary SULLIVAN. Yes, Mr. Natcher. That agency is responsible for several functions. First of all, we have had for a number of

years the National Centers for Health Services Research that has been operating at the Centers for Disease Control as well as on the NIH campus. Health Services Research will become part of this new agency, and effectiveness research that we are committed to will also be a part of that.

That research effort is going to be important in helping us learn which of the many procedures for treating patients are really effective, and which are not. One of the projects that they are reviewing, for example, is the efficacy of coronary bypass operations, that is a major procedure that is done around the country.

Other studies are researching the effectiveness of transurethral prostactomy for an enlarged prostate, hip replacement surgery, and a number of other things.

Our request for 1991 is an increase of $11 million, which would bring our effectiveness research up to around $47 million. We anticipate that this effort is going to continue to grow over the years. It will not only help us improve the quality of care we give to our citizens, but also help us in saving dollars. When we learn that a procedure is not effective, we will disseminate that information to the medical community, so that procedure will not be done.

The agency will be a division within the Public Health Service and its Director will report to Dr. Mason, our Assistant Secretary for Health.

Mr. NATCHER. As I understand the budget for the new agency, it is financed in large part from transfers from the Public Health Service evaluation funds. What effect will this have, Mr. Secretary, on other agencies in the Public Health Service. What effect will this have, especially as to NIH, Mr. Secretary?

Secretary SULLIVAN. Mr. Chairman, there are several trust fund transfers. The total budget for the agency will be around $110 million. It will not have an adverse effect on NIH, because those dollars that are for evaluation are in the budget for the National Center for Health Services Research. In other words, what has happened is that that center has now been subsumed into our new health policy agency.

They are the ones who tell us, of course, about the National history of disorders such as coronary artery diseases, or the effectiveness of, say, a drug like TPA, or a treatment of coronary insufficiency as compared with coronary bypass surgery. It is not taking dollars away from NIH, but simply taking a functioning unit and making it a part of this new agency.

Mr. NATCHER. When you get the transcript back, Mr. Secretary, will you amplify that just a little as to your entire statement? It will help us on our committee if you will.

[The information follows:]

AGENCY FOR HEALTH CARE POLICY AND RESEARCH

The 1991 budget request for the Agency for Health Care Policy and Research (AHCPR) includes an estimated $41 million to be derived from the PHS one percent evaluation fund. This represents 40 percent of total evaluation funds, as authorized in the Omnibus Budget Reconciliation Act (OBRA) of 1989. As in previous years, these funds will continue to support the National Medical Expenditure Survey (NMES) and the Hospital Studies Program (HSP) as well as new expanded health services and medical treatment effectiveness research. These funds are in addition to our request of $39 million in general fund budget authority, $29 million in Medi-

care trust fund transfers, and $1 million available through the NIH for National Research Service Awards for a total AHCPR program level of $110 million.

We believe the programs of the AHCPR are of highest priority for producing information which will lead to reform of the nation's health care system. We fully support a total program level of $99 million in 1990 and $110 million in 1991 to accelerate the ability of the AHCPR to gather and analyze the data necessary to help understand current medical expenditures and to assist those in leadership positions make better informed decisions about national health care policy.

Since OBRA 1989 authorized the use of 40 percent of the funds for the AHCPR on December 19, 1989, only about two months ago, we are still evaluating the effect on other agencies of the PHS. However, as part of the AHCPR effort, a PHS coordinating body, with representatives from the NIH, ADAMHA, and other PHS agencies, will work cooperatively to set the AHCPR research agenda. We expect there will be continual opportunities for studies to be performed by other agencies of the PHS through interagency agreements.

AGENCY FOR HEALTH CARE POLICY AND RESEARCH

[Dollars in millions]

	1989	1990	1991
Budget information:			
AHCPR:			
NMES	10.0	11.2	10.2
HSP		3.5	3.5
HSR&TA	5.3	21.1	20.5
MTEP		5.7	6.5
Undistributed			3.2
Subtotal	15.3	41.5	43.9
NCHS:			
Vital statistics		7.6	7.6
Nat'l Hlth Int'view		1.5	1.5
NHANES	10.4	7.1	7.1
Nat'l Hlth C Svy		2.8	2.8
Data/other	1.9		
Subtotal	12.3	19.0	19.0
OASH	3.2	3.0	3.1
ASPE	6.0	6.9	7.0
Undistributed	61.2	33.2	36.8
Total available	98.0	103.6	109.8

Note.—Chart based on best information currently available. Since the 1991 budget was formulated before 1990 enactment, the amount budgeted for AHCPR (40 percent of total available) is an estimate. Total amount available in 1991 has been revised by the Office of Budget (ASMB), to more nearly reflect actual availability.

DRUG TREATMENT SYSTEM

Mr. NATCHER. Now, as far as drug abuse is concerned, both the Congress and the President have expanded funding for drug abuse programs over the last several years, as you well know. I personally like Bill Bennett, Mr. Secretary. I think he is an able man. What is your personal evaluation of the drug treatment system as it exists in this country today?

Secretary SULLIVAN. Mr. Chairman. I think the President's drug strategy, which my Department played a key role in developing, with specific concentration on the demand reduction aspects, is a good one.

Director Bennett has emphasized, as he has spoken around the country, both components of the plan, or really three components. One component is interdiction, that is trying to prevent drugs from

reaching our borders and roughly about one-third of the dollars in the President's plan address that. Another third has been targeted for law enforcement activities in our country, and the other third is dedicated to demand reduction. That last third is our portion.

We have a total of $1.7 billion in our budget for demand reduction efforts. Of that $1.7 billion, slightly more than $1 billion is for treatment activities. We have actually doubled the dollars from $569 million in 1989 to a little more than $1 billion in our 1991 budget for treatment, which will expand the number of treatment slots available.

In addition, we have research at the Alcohol, Drug Abuse, and Mental Health Administration under the direction of Drs. Goodwin, Judd, and Schuster, and their colleagues, to find better treatment. Widely varying success rates for treatments have been reported, some as low as ten percent and others as high as 70 percent. I don't have firm figures however.

Most individuals in the field tell me the success rate averages 20 to 30 percent with the current treatment methods. We need to find better methods of treatment. Research that is underway at ADAMHA will help us. We have about $300 million for drug treatment research there.

In the fall of 1989, a new unit was established in ADAMHA, a unit for drug treatment. It is headed up by Dr. Beny Primm, a nationally recognized drug treatment expert. His role is to work with centers around the country in developing treatment programs.

One of the problems is that in spite of the doubling of the dollars over the last two years, we are running into problems getting communities to help us establish drug treatment facilities. We need to have facilities in the community and not across town because those individuals who are addicts, who need treatment, need to have it close by.

A good example of what I mean is in New York. New York City had a drug treatment facility down in the Battery for all of Manhattan. You can imagine someone who needed a drug treatment program going from 135th Street down to the Battery two or three times a day. That is totally impracticable.

Communities resist having facilities located in their neighborhoods, because of the fear of crime, et cetera. Clearly, we need to get better cooperation from our communities so that we can establish these facilities. We have the dollars, but dollars are only part of the answer.

Another thing we are doing with the increased dollars is working to get more trained personnel. From the standpoint of treatment, we have a number of efforts under way. We are very encouraged, but to give you as accurate a picture as I can, I think it is fair to say that we still don't feel that we have the best arrangement or the most optimal treatment.

Hopefully, studies from our research laboratories in the near future, will identify better treatments than we have had. Funding for prevention and education is significant, about $500 million, because we want to do everything possible to discourage young people from getting involved with drugs. Last April we were pleased to announce the results of a high school senior survey conducted in 1988, which showed that compared to 1985, we had a 33 percent re-

duction in the number of casual drug users—that means individuals who had used a drug at least one time in the past 30 days. That was the first time we had seen that dramatic a drop.

At the same time we saw that, we unfortunately also saw a 25 percent increase in the number of hard core users—that is addicts. Those are the individuals who are associated with crack and inner city violence. So in the drug war against the casual users, we feel we have turned the corner. Dr. Bennett participated with me in the conference to make that announcement. But for the hard core users, we still have a long way to go. We want to have a full court press on that for some time.

Mr. NATCHER. Mr. Smith.

DRUG REHABILITATION

Mr. SMITH. I think it is one of the most thorough answers I have heard and it squares with everything I have heard. I wonder if you may have more statistics. You referred to the number who stay off of drugs for, I assume three years. Is that considered to be a cure, rehabilitated? What time is necessary?

Secretary SULLIVAN. Yes, the phrase we use is "drug free," because of the fact that we emphasize that addiction is a chronic disease, something like Alcoholics Anonymous. They never call themselves cured, but indeed the criteria do vary according to the facilities. That is one of the things we need to do—get some uniformity of definition here. But certainly being "drug free" for a year or longer is a minimum.

Mr. SMITH. That was the criteria you were using in saying that 10 to 30 percent of those who go into rehabilitation?

Secretary SULLIVAN. Twenty to thirty percent. Ten percent is the low figure of all the data that has been gathered. Seventy percent is the high figure. We have some reservations about the accuracy of the high figures. It depends on the quality of the data—how good the data collection is.

Mr. SMITH. What period of time would the average period of rehabilitation be, 30 days or longer?

Secretary SULLIVAN. Twenty eight to thirty days is the standard period. We have to be prepared for relapses to occur. That is why we emphasize that this is a chronic disorder so that we have these programs hoping that one cycle of treatment would be effective but really committed to the fact that it may take more than one cycle. This is comparable to, say, other chronic disorders such as someone with diabetes. It may take a period of time before the right dosage of insulin is identified. So it may take two or three cycles of treatment to get further help.

Mr. SMITH. Do you have a figure for what the average cost is per person who is considered to have stayed in the program long enough to be drug free—that is, one year?

Secretary SULLIVAN. I will have to get back to you. I know that it varies among the facilities, but I would like to get back to you with the range of costs and what the average is.

[The information follows]

DRUG REHABILITATION COSTS

We do not have the precise information necessary to determine the average cost per person to remain in a program long enough to be considered rehabilitated. However, we do know that the longer a person remains in treatment the longer they abstain from drug use. Currently there are a number of different methods for treating drug abusers including detoxification, maintenance programs, drug free programs, and residential treatment programs. Each treatment method has varying lengths of treatment and costs on average vary between $3,000 and $26,000. Most people receive inpatient treatment for a period of 28 days. Chronic relapse is normal and individuals often go through 3 or 4 treatment episodes before becoming abstinent for long periods of time. Inpatient treatment slots can serve approximately 2.5 persons a year.

We are conducting studies which compare the efficiency of the different methods of treatment by matching patients to specific treatments. Through the National Drug and Alcoholism Treatment Unit Survey (NDATUS), which is now being conducted on an annual basis, and expansion of the Drug Abuse Treatment Outcome Survey (DATOS), we will be collecting information on who is in treatment, what types of treatment, and response rates to treatment. The Department is currently reviewing the issue of what legally constitutes being "rehabilitated".

Mr. SMITH. I know one facility, a 30 day program—and the money is paid up front usually by an employer—I think it is $12,000. The majority, of course, don't stay even three weeks. But anyway, to make a long story short, per person who is actually rehabilitated, for whom the fee has been paid, it turns out to be a total cost of about $43,000 per person rehabilitated. Does that sound like the figures you have heard?

Secretary SULLIVAN. That would not be surprising. I know that some treatment facilities, at least as of about two years ago, that were on the low side were running around $4,000 for a 28 to 30 day period of treatment. But figures of $10,000 or $12,000 certainly are not unusual.

Mr. SMITH. I mean the $43,000 figure?

Secretary SULLIVAN. Yes. That figure could be accurate. It would include, as you phrase it, the numbers of individuals who are really cured by taking into account the relapse rate.

Mr. SMITH. Who successfully completed?

Secretary SULLIVAN. Yes, right.

Mr. SMITH. We certainly do need, as you indicated, to look at these various programs and find out how it can be done. If it costs $43,000 for a 30 day treatment for those who successfully completed and only 20 to 30 percent completed, we are never going to solve the drug problem with a rehab program. We need some work done in this area. As we are spending a lot of money in this area, we need to do a lot of work in figuring out a rehab program, don't we?

Secretary SULLIVAN. That is absolutely correct, Mr. Smith.

One of the promising things underway at the National Alcohol, Drug Abuse and Mental Health Administration is work on a tricyclic compound called Dabibpramine, which seems to decrease the craving for drugs among those who are addicted. We hope the work with that drug will prove to be successful. If it is, it could be very helpful in improving the rate of successful treatment outcomes. If that happens, we may see some remarkable declines in the cost of treatment, but it is too soon for us to say.

Mr. NATCHER. I have one.

Mr. SMITH. I have one more short question. Do you have any states that indicate the success rate in voluntary programs com-

pared to what I would call involuntary programs? In other words, persons who are on parole, who are under some pressure to complete the program?

Secretary SULLIVAN. No, I don't have that data with me, but I will be happy to consult with our drug treatment experts and get a response back to you.

Mr. SMITH. Thank you.

[The information follows:]

COMPARISON OF DRUG TREATMENT PROGRAM SUCCESS RATES

While we have no systematic comparison of success rates between voluntary and involuntary treatment, a few studies have been conducted through NIDA's extramural research program. These studies show basically the same rate of success for voluntary and involuntary participants. In some cases, a slightly better success rate exists for involuntary clients due to the threat of mandatory urine testing.

INFANT MORTALITY

Mr. NATCHER. Mr. Secretary, according to the budget documents that we have before the committee at this time, there is an increase of $369 million for programs directed at reducing infant mortality rates. You know, for several years the Department announced and then abandoned, to a certain extent, specific goals for reducing the infant mortality rate by the year 2000. We would hear quite a bit about it. Mr. Stokes, you will recall, from time to time over the years, they would come in and talk with us about it.

What do you hope to achieve, Mr. Secretary, in the next ten years in terms of the overall infant death rate and the specific rate for minorities?

Secretary SULLIVAN. Mr. Chairman, as I mentioned earlier today, the United States ranks 18th among the industrialized nations in the infant mortality rate with a rate of 9.9 infant deaths per thousand live births. That is in spite of the fact that we are number one in our per capita expenditures for health care. We spend more than $2,000 per capita on health care costs for our citizens and the next country to the United States is Canada, with $1,400. They spend one third less than we do, yet they have a lower infant mortality rate. Japan is number one, with a rate of six deaths per thousand live births.

At the end of world War II the United States had a much lower infant mortality rate than Japan. Japan's rate was very high. The Japanese Government and health officials undertook a concerted effort to bring that rate down, and it has succeeded. Outreach programs, make sure that every pregnant mother gets prenatal care, and gets into the system early. That has paid off.

Our infant mortality initiative is designed to do just that. There is no mystery about this. We know what factors contribute to this, and cause it. It really means getting mothers in for prenatal care early on. There are some problems that are complicating this, such as the problem of drug and alcohol abuse.

As you may have heard, on some of our Indian reservations where alcoholism is a severe problem, we have a high incidence of what we call fetal alcohol syndrome. Infants born of mothers who are alcoholic are born with impaired development of their brains and their central nervous systems, and with mental retardation. Of

course there is a high infant mortality rate in that group. On our reservations the fetal alcohol syndrome is as high as 25 percent—it affects one in every four babies born.

What that means, obviously, is individuals who are never going to reach their full potential and may require custodial care all of their lives. Therefore, the human tragedy is compounded by the economic costs of institutional care for those individuals.

Our infant mortality initiatives also intersect so many other health issues, such as drug abuse with crack babies, the problem of AIDS, the babies born with AIDS, and the fetal alcohol syndrome.

The Public Health Service believes we can, by the year 2000, have substantial improvements in lowering our infant mortality rate. I cannot recall the figure, but I believe it is somewhere around six or seven infant deaths per thousand live births by 2000. We feel this is a goal that can be reached. I will check with the Public Health Service people and if the figure is incorrect, I will get the accurate figure back to you.

Our initiative encompasses a broad array of activities. It gives more support through our community and migrant health centers, where we have particular problems.

It also gives additional support in our Indian health centers. It includes such things as I think a $2 million effort for what we call "Mom Vans". People in low income communities often don't have transportation. Where there is a need, we believe it is a good investment to have vans pick up expectant mothers, bring them to the clinic for the care they need, and then return them home.

Our experts have estimated that about $400 invested in seeing that each mother has good prenatal care will not only lower our infant mortality rate, but will save us tens of thousands of dollars we are now paying for care at $1,000 to $2,000 a day for keeping premies weighing one or two pounds alive, in our neonatal intensive care units.

We believe a good investment here represents prevention, as well as contains health care costs, and gives us citizens that we need to become productive leaders and members of our work force in the future.

Mr. NATCHER. Mr. Secretary, we would appreciate it if you would have inserted in the record at this point a table showing the change in infant mortality rates over the last ten years broken down to show specific rates for high risk groups.

[The information follows:]

U.S. INFANT MORTALITY RATES

[Per 1,000 live births]

Year	Total	White	Nonwhite	
			All nonwhite	Black
1977	14.1	12.3	21.7	23.6
1978	13.8	12.0	21.1	23.1
1979	13.1	11.4	19.8	21.8
1980	12.6	11.0	19.1	21.4
1981	11.9	10.5	17.8	20.0
1982	11.5	10.1	17.3	19.6
1983	11.2	9.7	16.8	19.2

U.S. INFANT MORTALITY RATES—Continued

[Per 1,000 live births]

Year	Total	White	Nonwhite	
			All nonwhite	Black
1984	10.8	9.4	16.1	18.4
1985	10.6	9.3	15.8	1,8.2
1986	10.4	8.9	15.7	18.0
1987	10.1	8.6	15.4	17.9
1988 [1]	9.9	N/A	N/A	N/A

[1] Provisional.

Mr. Secretary, of course we have many more questions pertaining to your budget. These will be taken up with your department heads when your department heads appear before our subcommittee, the agency heads and all.

But, in finishing as far as today is concerned, I want to commend you. I think this has been an excellent hearing. Mr. Secretary, you have in your department as many well qualified and able people as any department in the Government. I believe that. If I did not believe it, Mr. Secretary, I would not say it. Your department has all kinds of people that are qualified and able.

Yesterday, during the overview hearings with the Secretary of the Treasury, the Director of OMB, the question of Gorbachev arose for some reason or another, and the Time Magazine cover, the Man of the Decade. I said to them, I would never have placed him on the cover of Time Magazine. If they asked me for the man of the decade I could name you five or six people in your department that I could put on there.

Secretary SULLIVAN. I agree, sir.

Mr. NATCHER. Mr. Smith, do you have additional questions?

Mr. SMITH. No, thank you, Mr. Chairman.

Mr. NATCHER. Mr. Stokes, do you have additional questions?

INFANT MORTALITY—ONE STOP SHOPPING

Mr. STOKES. Thank you very much.

Just to follow up on the Chairman's questions relative to infant mortality, I notice you have a new infant mortality initiative, a $25 million one-stop shopping proposal to be carried out through the maternal and child health program. Can you tell us what that is?

Secretary SULLIVAN. Mr. Stokes, that is part of our overall outreach effort. Low income pregnant women who need health services oftentimes need a number of other services as well, such as food stamps through the Women, Infants, and Children (WIC) program in Agriculture, child care services, and others. The way these services are often organized requires that recipients go to multiple sites for assistance. These may even be located in different parts of town. These individuals often do not have transportation, or depend upon public transportation, and may have two or three children at home. What would seem to the average citizen to be very easy and straightforward is a major undertaking for these women.

I think this is one of the reasons a number of mothers don't get prenatal care. The one stop shopping initiative is designed to co-

ordinate a number of services, co-locating them in one place. When a mother comes in, she will get, not only her eligibility for Medicaid, but her WIC eligibility determined, her child care needs addressed, and the whole array of support services. That will make it convenient for her. Rather than having to go to different places and maybe on different days, she will come to that one site.

This is intended as a demonstration project to see if we can successfully organize the various services not only provided by my Department, but also the Department of Agriculture, the Department of Education, the Department of Labor, et cetera. We think that this holds great promise for improving our outreach services. The way it is now organized often serves as a barrier to people who need services.

ADDRESSING THE DRUG PROBLEM

Mr. STOKES. That approach makes a lot of sense to me.

Let me go back to the drug problem for a moment and sort of think out loud with you. I don't have any doubt about the fact that the President has a commitment to the drug problem in this country. He has gone on national TV. He has asked the Congress to give him somewhere in the neighborhood of $9 billion for the program. You have approximately $1.7 billion in your part of the budget for drug treatment and prevention programs.

Ordinarily this amount of money would be sufficient to treat any type of problem, but we are talking about an epidemic in this country. The crack problem alone in the cities and suburbs throughout America is indicative of the fact that our nation has a very severe addiction problem.

I don't know what the answers are, but I do know that for a long time we avoided really looking at this problem the way it is. We let the media, through our television sets at night show young men in the inner city up against a police car being searched and portraying this as being indicative of the problem of drugs in this country, when we know that is not the problem.

Drugs are endemic in this society and have spread throughout every elementary school, high school, every college, and every suburban community, in addition to every inner city. I just wonder if we are really looking at the whole problem of addiction, and if we are ever going to try and arrest this problem and find solutions?

Are we really utilizing the structures we have now through ADAMHA or any other national center? Are we really concentrating on the problem of addiction in this society?

Secretary SULLIVAN. Mr. Stokes, I think that the question really is a very fundamental one. Why is it that we have such a severe problem with addiction? We still have a problem with alcohol, but we seem to have phases where we go from one drug to another as a favorite drug of addiction.

This gets into other areas that we are concerned about. My Department is concerned about them because I maintain that the first, original, and still the best, Department of Health and Human Services is the family. We have a severe problem in our country with the instability of the family. We have high incidence of single

parents, of children born out of wedlock, where two parents are not present.

That leads to high incidence of poverty. Where you have such a high number of female heads of households, it means that in addition to the loss of the earning capacity of the absent father, you also have the loss of that mentoring function and role which the father plays in the family.

That gives rise to, or is fertile ground for, a whole range of social pathology, of which addiction is but one. That is not the whole answer, because we see unfortunately, problems of addiction arising in some of the most stable, successful families.

The fundamental question is: Why is it that we as a society consume most of the illicit drugs that are available around the world? I don't think we have found the complete answer to that.

I know that part of the answer is to do everything that we can to strengthen the family. This is why we have emphasized programs in our Department for foster care and adoption services to try and provide loving, supporting homes for our children who are victimized by the instabilities of our families. We also need to strengthen our communities and do everything we can to keep our families together.

Those are simply some observations I will offer without saying we have the real answer, but we need to do everything we can to try to find the answer. That is a fundamental issue that contributes to so many of the problems that we are trying to address in our Department.

THE DRUG PROBLEM

Mr. STOKES. I appreciate your comments. I commend you on your selection of people like Dr. Beny Primm, who is undoubtedly one of the top experts in the country in the field of drug treatment.

Long before they get to Dr. Primm and treatment, there are some basic rudimentary problems that are here that we need to be looking at very closely and carefully if we are really to solve the problem and not just treat it. We need to get to the root causes of it. No matter how much you condemn Colombia, Thailand, and other parts of the world for sending illegal and illicit drugs into this country, if there was not a demand for them, they could not do it. The same basic principles of economics apply here. There is both supply and demand.

It seems to me at some point in time we must pay some attention to the root causes of why there is such a great demand for drugs in this country.

Let me close by joining with all of the others in saying what a pleasure it is to have you come before this committee. I have sat on this committee for about 20 years. You are the only Secretary I have seen come before this committee and address all the questions posed relative to the budget in that department in the way that you have done with a thorough, keen analytical knowledge of your budget and your department. It is a pleasure to see it. I commend you for it.

Thank you very much.

Mr. NATCHER. Mr. Secretary, we want to thank you for your appearance before our committee at this time. This has been an excellent hearing, Mr. Secretary.

The committee will now adjourn until 10 o'clock, February 20th, at which time we will have the Secretary of Education before the committee.

[The following additional questions were submitted to the Secretary to be answered for the record:]

SEQUESTRATION FY 1990

Mr. Natcher: Mr. Secretary, would you describe for the Subcommittee the overall impact of the FY 1990 sequestration on your Department and give us a few examples of the areas which were hit the hardest?

Secretary Sullivan: The deficit target for FY 1990 was $100 billion. A sequestration of $16.2 billion was required to reach the deficit target, a 5.3 percent reduction for non-defense programs and a 4.3 percent reduction for defense programs. The Reconciliation Act reduced that amount to $5.7 billion or the equivalent of a full sequester for 130 days.

This $5.7 billion reduction was achieved by a full-year across-the-board reduction of 1.4 percent for non-defense programs, and 1.5 percent of defense programs.

For HHS programs, the revised sequester order equated to a $1.5 billion reduction in budget authority and a $1.3 billion reduction in outlays. However, given the hold harmless provisions of the Gramm-Rudman-Hollings act, the Department realized only a $0.3 billion reduction in BA and $0.7 billion in outlays.

As stated before, a uniform percentage reduction was taken from all programs, except when the hold harmless provisions took effect. Therefore, even though the actual reduction is greater for some programs, the effect was even across-the-board. The reductions for discretionary programs under the jurisdiction of this Subcommittee follows:

(In millions of dollars)

	Enacted Program Level	Sequester Realized	Available Budgetary Resources
PHS:			
HRSA.....	$1,770	$23	$1,747
CDC.....	1,105	14	1,091
NIH.....	7,673	97	7,576
ADAMHA.....	2,671	27	2,644
OASH.....	110	1	109
Total PHS.....	3,329	162	13,167
HCFA.....	1,972	26	1,946
SSA (LAE).....	3,837	--	3,837
FSA.....	2,239	3	2,236
OHDS.....	2,807	37	2,770
OS.....	233	2	231
Total, L/HHS...	24,417	230	24,188

Mr. Natcher: Insert in the record if you would at this point a short list showing the major reductions required under the sequestration process for FY 1990.

Secretary Sullivan: As stated above an across-the-board percentage reduction of 1.4 percent was applied to all programs not exempt in the Gramm-Rudman-Hollings Act.

A list of programs that are fully exempt and Special Rule Authority, are listed below:

Fully exempt:
- Social Security Benefits (OASDI)
- Medicaid
- Aid to Families with Dependent Children (AFDC)
- Supplemental Security Income (SSI)
- Special Benefits for Disabled Coal Miners
- Retirement Pay & Medical Benefits for Commissioned Officers
- Medical Facilities Guarantee & Loan Fund
- Health Professions Graduate Student Loan Fund
- Payments to Health Care Trust Funds
- Payments to Social Security Trust Funds
- Health Education Loans (prior Legal obligations, only)

Special Rules:

Medicare

Part A: 2.092 percent through December 31, 1989; 1.46 percent thereafter, offset by a special reconciliation provision increasing the post-sequester, post-December 31 incurred cost by 1.42 percent.

Part B: 2.092 percent through March 31, 1990; 1.46 percent thereafter.

Foster Care & Adoption Assistance
100 percent of the increases in State foster care maintenance and adoption assistance payment rates for FY 1990.

Community Health Centers
1.4 percent.

Migrant Health
1.4 percent.

AGENCY FOR HEALTH CARE POLICY AND RESEARCH

Mr. Natcher: As we understand the budget for this new agency, it is financed in large part through transfers from the Public Health Service evaluation funds. What effect will this have on other agencies of the Public Health Service such as the National Institutes of Health?

Secretary Sullivan: The 1991 budget request of $110 million for the Agency for Health Care Policy and Research (AHCPR) includes an estimated $41 million to be derived from the PHS one percent evaluation funds. Since OBRA 1989 authorized the use of 40% of the total fund for the AHCPR on December 19, 1989, only about two months ago, we are still evaluating the effect on other agencies of the PHS. However, as part of the AHCPR effort, a PHS coordinating body, with representatives from the NIH, ADAMHA, and other PHS agencies, will work cooperatively to set the AHCPR research agenda. We expect there will be continual opportunities for studies to be performed by other agencies of the PHS through interagency agreements.

Mr. Natcher: Can you tell us how much has been spent traditionally on evaluation studies at the Department and how this changes in 1990 and 1991 under the new financing arrangement for medical treatment effectiveness?

Secretary Sullivan: Traditionally, at the beginning of a fiscal year, a portion of the one percent evaluation funds have been earmarked for specific PHS evaluation projects. The total available for use has been approximately $100 million for several years. In 1990 and 1991, as a result of the 40% tap authorized by OBRA 1989, an additional 20% of the funds are earmarked for AHCPR at the beginning of the fiscal year. We still estimate that approximately 30% of the total fund will remain undistributed and will be returned to the contributing PHS agencies in 1990 and 1991.

As in previous years, these evaluation funds will continue to support the National Medical Expenditure Survey (NMES) and the Hospital Studies Program (HSP) as well as support new expanded health services and medical treatment effectiveness research.

Mr. Natcher: Mr. Secretary, in your view would it be better to finance this new agency through direct appropriations rather than through taps of the Public Health Service evaluation funds?

Secretary Sullivan: We believe the programs of the AHCPR are of highest priority for producing information which will lead to reform of the nation's health care system. We fully support a total program level of $99 million in 1990 and $110 million in 1991 to accelerate the ability of the AHCPR to gather and analyze the data necessary to help understand current medical expenditures and to assist those in leadership positions make better informed decisions about national health care policy.

As I stated earlier, OBRA 1989 authorized the use of 40% of the total fund by the AHCPR on December 19, 1989, only about two months ago. We are still evaluating the effect of this funding arrangement on other agencies of the PHS. However, we believe that one beneficial outcome of this provision has been the creation of a PHS coordinating body, comprised of representatives from the NIH, ADAMHA, and other PHS agencies, which will cooperatively work with the AHCPR to set a research and evaluation agenda. We expect, therefore, that there will be continual opportunities for studies to be performed by other agencies of the PHS through interagency agreements.

REFUGEE RESETTLEMENT

Mr. Natcher: Does the Administration plan to propose any significant changes in the refugee authorization law?

Mr. Secretary: Since authorization for the refugee programs expired on September 30, 1988, the refugee resettlement program has continued to operate based on the authority provided in the annual appropriations act. The Administration has not proposed any changes to the authorization this fiscal year.

SSA AS AN INDEPENDENT AGENCY

Mr. Natcher: Last year, as part of the budget reconciliation action, the House passed a measure that would make SSA an independent federal agency. What is your position on this proposal?

Secretary Sullivan: I do not support taking SSA out of the Department of Health and Human Services and making it an independent agency. To carry out its mission of providing effective and efficient public service, SSA must stay clearly

focused on that goal, be well managed, motivate and meet the needs of its employees, and obtain sufficient resources. This has been and can continue to be done within HHS. Independent agency status would not make the task any easier and, indeed, is squarely against recognized concepts of good management. Further, separating SSA from HHS would undercut the President's role as manager of the executive branch, weaken SSA's important links with health and social services programs for the aged administered by other HHS agencies, and eliminate many administrative economies inherent in a large government department.

DEPARTMENTAL REORGANIZATIONS

Mr. Natcher: Are you planning any significant reorganizations in the Department during the next year ?

Secretary Sullivan: There are three reorganizations planned:

1. Public Health Service - Centralize the functions of the Regional Health Administrators in PHS headquarters.

2. Health Care Financing Administration - Create a Medicaid Bureau within HCFA.

3. Public Health Service - Create two Bureaus relating to maternal and child health services.

HOMELESS

Mr. Natcher: Mr. Secretary, it has been almost three years since the passage of the McKinney Act to help the homeless. What do we know today that we didn't know in 1987 about the extent and causes of this problem?

Secretary Sullivan: Several major studies have increased our knowledge about both the extent of homelesseness and the demographics of this population. There are approximately 650 thousand homeless on any given night. About 85% of the homeless are male and about 23% are members of homeless families. Problems which affect large numbers of homeless are unemployment (only about 20% of the homeless are employed), serious mental illness (30%), and substance abuse (30% - 40%). While deinstitutionalization has made some contribution to the problem of homelessness, 75% of the homeless have never been in a psychiatric

hospital. As a result of these findings, we are placing a greater emphasis on combining basic shelter assistance with counseling and treatment services to enable the homeless to become self sufficient.

Mr. Natcher: What do you see as the long-term prognosis for dealing with the problem of homelessness in this country?

Secretary Sullivan: Ultimately, the solution to homelessness lies in removing the barriers to self support for the homeless and by providing services which include education and training. Programs such as Head Start and JOBS will help the poor to become self supporting and thereby reduce the chances of their ever becoming homeless. For those who are homeless already, the Federal government will work with state and local governments, and with the private and non-profit sectors, to provide the services necessary for the homeless to achieve self support. Secretary Kemp and I recently signed a Memorandum of Understanding which will make it easier for the same grantees to provide both shelter services (primarily funded by HUD) and treatment services (primarily funded by HHS). In recognition of the homeless problem, and in response to it, funding for the homeless from the public, private, and non-profit sector, increased significantly from $300 million in 1984 to $1.5 billion in 1988.

FLUORIDATION

Mr. Natcher: Mr Secretary, the National toxicology Program recently released a study raising questions about the safety of water fluoridation programs. What is your view of this finding and what actions are expected to be taken by the federal government in response to the study?

Secretary Sullivan: First of all, I can assure you, that after 45 years of water fluoridation, and scores of human epidemiological studies in the U.S. and abroad, we have uncovered no evidence of a relationship between fluoridation and cancer, or any other disease. The National Toxicology Program has released <u>preliminary</u> data from a study on the possibility of a relationship between sodium fluoride and cancer in animals. The two-year study exposed rats and mice to <u>extremely high</u> does of sodium fluoride. This high level of exposure allows researchers to detect rare events. During the course of the study, five cases of bone cancer were found in male rats.

I must emphasize that this study is not yet complete. Data has yet to be fully analyzed or interpreted by the study scientists. In addition, the findings have not been reviewed by outside scientists. This process will not be complete until the end of April. In the mean time, the Assistant Secretary for health has formed a committee to review the scientific literature on the risks and benefits of fluoridation, to provide monthly interim reports, and to prepare a final report with recommendations by July 15.

Water fluoridation has proven highly effective in reducing tooth decay and thus improving the nation's dental health. Until the completion of the sodium fluoride study and the ASH's review of fluoride related scientific data, the many benefits of fluoride warrant continuation of present policy with respect to water fluoridation.

Mr. Natcher: How much money is budgeted throughout the federal government for water fluoridation activities?

Secretary Sullivan: The request for the National Institutes of Health includes $3.2 million for research related to fluoride. This research is conducted by the National Institute on Dental Research and the National Institute on Environmental Health Sciences. Through the Preventive Health Services Block Grant, the Centers for Disease Control (CDC) provides States with funds which can be used to fluoridate drinking water. We do not collect information on how many States use block grant funds for this purpose. Approximately $870,000 supports CDC staff who also provide technical assistance to States on fluoridating community and school water systems.

DEPARTMENTAL STAFFING

Mr. Natcher: The 1991 request reverses a decade long trend of staff reduction at the Department of Health and Human Services by proposing FTE increases for both 1990 and 1991. The combined increase for these two years is a 5,600 FTE increase over the level proposed in the 1990 President's Budget. We understand this results from a new policy at OMB to allow Departments more flexibility on staffing. Are these numbers accurate?

Secretary Sullivan: The 1990 President's Budget requested 114,000 FTE; the 1991 President's

Budget requests 119,606, an increase of 5,606 FTE. Of this amount, 2,714 or 48% represents real staffing levels for the Indian Health Service, which by law cannot be constrained by FTE ceilings.

For programs under the jurisdiction of this Subcommittee the 1990 request was 96,446; for FY 1991, our request totals 98,389, an increase of 1,943 FTE. The revised projection for 1990 included in the 1991 President's Budget is 97,508, 1,062 higher than in the 1990 President's Budget.

The following table displays this FTE data:

	1990 Pres. Budget	Change	1990 Revised Pres. Bud.	Change	1991 President's Budget
PHS.	22,394	1,450	23,844	422	24,266
HCFA	4,017	--	4,017	110	4,127
SSA.	63,731	-507	63,224	375	63,599
FSA.	1,029	--	1,029	--	1,029
OHDS	1,004	-4	1,000	--	1,000
OS..	4,271	123	4,394	-26	4,368
Total	96,446	1,062	97,508	881	98,389

Mr. Natcher: What controls are in place to monitor and manage staffing levels within the Department? Will this be left to agency heads such as the Director at NIH?

Secretary Sullivan: OMB Circular A-34 requires HHS to prepare a staffing plan based on estimates included in the President's Budget.

In addition, the Secretary requires quarterly reports on actual usage compared to the staffing plan. These reports are analyzed, and if necessary corrective action is taken.

The Office of the Secretary maintains an automated FTE system, called MERTI (Monthly Employment Retrieval Tracking Inventory). This system uses payroll data and compares actual and projected usage with budgeted FTE levels.

SURVEY AND CERTIFICATION

Mr. Natcher: $510 million is expected to be derived from user fees in the Medicare survey and certification area alone. Would you describe how this program will work and also tell us whether the Department would continue to want this level of program activity if user fees are not approved by the Congress?

Secretary Sullivan: Recent Congressional actions have dramatically increased HCFA's survey and certification responsibilities in both the Medicare and Medicaid programs. OBRA 87 requires enhanced survey and certification activities in nursing facilities and home health agencies. The Clinical Laboratory Improvement Amendments (CLIA) of 1988 require that all clinical laboratories, including physicians office laboratories, be surveyed and issued a certificate. The 1991 request of $510 million represents the cumulative effect of these congressional mandates.

The Department's 1991 request proposes a consolidation of Medicare and Medicaid survey and certification activities into a single account. Following the precedent set by CLIA 88, the Department is proposing legislation that will authorize Medicare and Medicaid survey and certification activities to be financed through user fees assessed on the health facilities being surveyed. All providers requesting participation in the Medicare and Medicaid programs, and all providers requesting recertification in these programs, as well as all laboratories to be certified under CLIA 88 guidelines, will have to pay the proposed user fees. The amount of the user fee will be sufficient to cover all of the direct and indirect costs associated with these activities. Consequently, a portion of HCFA's administrative costs will also be funded through the user fees. Revenues generated through the proposed user fees will be placed into a Survey and Certification Revolving Fund from which all outlays will be made. This fee arrangement was designed to make standards enforcement self-supporting.

If the user fee proposal is not approved by the Congress, the same level of funding will be necessary to support the increases in activity. Except for the CLIA 88 workloads, for which the Congress has already approved user fees, all survey and certification activities would continue to be financed through a combination of general funds and trust fund monies.

USER FEES

Mr. Natcher: Include in the record at this point a detailed description of all user fees assumed in the 1991 budget. Also, include the general and trust fund cost by activity if these user fees are not enacted.

Secretary Sullivan: The 1991 President's Budget assumes user fees in FDA, HRSA, HCFA, and FSA. The Administration continues to believe that those who derive special financial benefits from a Government service should be charged for the costs of providing that service.

A table displaying these data follows:

	Budget Authority	User Fees	Program Level
L/HHS Programs:			
PHS:			
HRSA.....	1,556,822	1,974	1,558,796
HCFA:			
Program Mgmt....	1,904,050	248	1,904,298
Survey & Cert...	--	510,100	510,100
FSA:			
Program Admin...	77,200	2,000	79,200
Subtotal, L/HHS...		514,322	
Non-L/HHS Programs:			
PHS:			
FDA.....	527,997	157,175	685,172
Total, HHS.....		671,497	

Description

PHS, HRSA - This user fee will fund the Health Care Quality Data Bank. The data bank is a National system for the receipt, storage, and dissemination of information on paid medical malpractice judgments and settlements, sanctions taken by Boards of Medical Examiners, losses of membership in professional societies, and certain professional review actions taken by health care entities. Amendments to the Health Care Quality Improvement Act of 1986 in P.L. 100-177 provide for the collection of user fees to cover the costs of processing requests and providing such information to users of the data bank and provide relief to the data bank operator from any civil actions with respect to information provided under the law.

HCFA, Program Management - User fees are collected from Health Maintenance Organizations (HMOs) seeking Federal qualification are credited to this appropriation.

HCFA, Survey and Certification Revolving Fund - Starting in 1991, Medicare and Medicaid survey and certification activities, including all associated HCFA administrative expenses, will be financed

through fees assessed on providers and suppliers requesting certification. This would change the funding source from the Medicare Trust Funds and General Fund to the providers and suppliers themselves, and would reduce the deficit. The self-supporting method of financing Medicare and Medicaid survey and certification also follows the precedent set by CLIA 88.

FSA, Program Administration - This user fee is to pay for and continue the expansion of the Federal Parent Locator Service (FPLS). Under this approach, States that access the system pay for the benefits they receive.

PHS, FDA - User fees are proposed to pay for the cost of reviewing new product applications. These fees will be charged for reviewing pre-market applications for drugs, biologics, medical devices, food and color additives, post-market surveillance of generic drugs, and enhanced seafood inspections and certification.

GENERAL PROVISIONS

Mr. Natcher: Insert in the record at this point an explanation of each change being proposed in the Title II or Title V General Provisions related to HHS programs.

Secretary Sullivan: Included in the President's budget for fiscal year 1991 are recommendations for changes in General Provisions in the Labor, Health and Human Services, and Education, and Related Agencies appropriations bill. Explanations for these changes follow:

Title II

Sec. 208. This provision would be modified to limit basic pays, special pays, allowances for subsistence and basic allowances for quarters of the commissioned corps of the Public Health Service, to a level not to exceed 110 percent of Executive Level I annual rate of basic pay, thereby maintaining commensuration with related government salaries.

Sec. 209. This provision is proposed for deletion, as it limits flexibility in shifting resources between the Department of Health and Human Services and the Department of the Interior for the purposes of carrying out the Native American Programs Act.

Sec. 211. This provision is proposed for deletion, as it limits the Department's flexibility to allocate personnel resources.

Sec. 213. A one-time portion of this provision, which disallows transferring funds for HIV-related activities between appropriation accounts in FY 1990, is proposed for deletion. New language is inserted which provides that Congress shall be promptly notified of these transfers. (See Sec. 212.)

Sec. 214. This provision, which prohibits using Federal funds appropriated under this Act for any project which involves the capture or procurement of chimpanzees obtained from the wild, is proposed for deletion. The language duplicates existing regulation and provisions within the CITES (Convention on International Trade of Endangered Species) Treaty.

Sec. 218. This provision, a one-time provision naming various NIH facilities, is proposed for deletion.

Sec. 219. This provision, a one-time reduction associated with improved procurement practices in FY 1990, is proposed for deletion.

Sec. 220. This provision, which duplicates a provision in substantive law and existing administrative guidelines on AIDS education programs, is proposed for deletion.

Sec. 221. This provision is proposed for deletion, as it prohibits enforcing compliance with Federal law relating to Foster Care and other provisions of the Social Security Act.

Sec. 212. The adoption of this provision would allow the Secretary the flexibility to meet any unforeseen HIV-related resource needs through a transfer of up to 3 percent of funds appropriated for the Public Health Service (other than those for "Retirement Pay and Medical Benefits for Commissioned Officers") to any account of the Department which includes funds available for HIV-related activities, provided that the Congress is promptly notified of any such transfer.

Sec. 216. The adoption of this provision would simplify payments of user fees by States to the Family Support Administration (FSA) for services provided by the Office of Child Support Enforcement.

FSA grants Child Support Enforcement matching funds to States. Currently, States which use technical services offered by FSA (preparing and mailing tax offset notices) must send funds back to FSA's salaries and expenses account. This provision would simplify administration by allowing FSA to deduct from grants the costs of technical services States have requested, and then transfer these funds to the salaries and expenses account.

Title V

Sec. 512. This provision, a one-time provision relating to absorption of the 1990 pay raise, is proposed for deletion.

Sec. 514. This provision, which imposes a one-time limitation on expenditures for advisory and assistance services, is proposed for deletion.

Sec. 515. This provision, a one-time provision for transfers in FY 1990, is proposed for deletion.

Sec. 518. This provision, a one-time reduction in salaries and expenses, is proposed for deletion.

Sec. 519. This provision prohibits the Department from implementing a regulation relating to the reclassification of rural referral centers. It is proposed for deletion because the same prohibition was extended through FY 1991 in OBRA 1989, making this provision unnecessary.

Sec. 520. This one-time provision, which limits distribution of sterile needles, is proposed for deletion.

Mr. Natcher: What would be the impact on DHHS if section 201 related to State systems of personnel were deleted?

Secretary Sullivan: Section 201 disallows withholding grant-in-aid funds from states with merit systems because of disapproval of personnel, the selection of that personnel or their relative pay rates. There would be virtually no impact on the Department if this Section were deleted.

The original purpose of imposing Merit System requirements was to insure the impartial and efficient administration of Federal grant programs by State and local governments; however, these jurisdictions are just as interested as the Federal Government is in ensuring efficient and effective

use of grant funds. Additionally, all states have been certified as having merit systems at this point in time. It is unlikely that this Department would challenge this certification by withholding grant funds.

The Department has proposed deletion of this Provision in the past, as it was considered both unnecessary (for reasons stated above) and intrusive.

SUDDEN INFANT DEATH SYNDROME

Mr. Natcher: Please insert in the record at this point a consolidated table on Sudden Infant Death Syndrome (SIDS) spending throughout this Department.

Secretary Sullivan: Public Health Service funding for research on Sudden Infant Death Syndrome in FY 1991 is as follows:

NIH:	
National Institute on Neurological Disorders and Stroke	$3,098,000
National Institute on Child Health and Human Development	$39,400,000
Division of Research Resources	$840,000
Subtotal, NIH	$43,338,000
HRSA: Maternal and Child Health Block Grant program	$490,000
Total, SIDS Research	$43,828,000

ABORTION

Mr. Natcher: Insert in the record a detailed table on federally financed abortions by year and by cause from 1978.

Secretary Sullivan: Following the implementation on February 14, 1978, of regulations which resulted from the Hyde Amendment, a specific reporting procedure was developed for reporting information on Medicaid financed abortions and allowable abortion-related expenditures. Although the Health Care Financing Administration does maintain complete information on the number of abortions financed by the Medicaid program since 1978, they do not have this information by "cause" of the abortion.

Since February 14, 1978, 59,992 Medicaid financed abortions have been reported by forty-seven

jurisdictions through September 30, 1989. The table below represents the number of reported Medicaid abortions by fiscal year.

	FISCAL YEARS				
1978-1985*	1986	1987	1988	1989	TOTAL
59,527	232	91	94	48	59,992

* Data for FY 1978 are only for the period from February 14, 1978 through September 30, 1978.

STAFFING CHART

Mr. Natcher: Insert in the record at this point a ten year table of FTE use within the Department similar to the one on page 104 of last years hearings.

Secretary Sullivan: The information follows:

DEPARTMENT OF HEALTH AND HUMAN SERVICES
STAFFING - FY 1980-1991

	ACTUAL FTE USAGE								PRES. BUDGET	
	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991
PHS:										
FDA	7,316	7,293	7,257	7,190	7,001	6,961	7,210	7,398	7,877	8,444
HRSA	5,359	4,738	4,008	3,414	2,948	2,399	2,250	2,181	2,161	1,956
IHS	10,283	10,309	11,035	11,554	11,538	11,616	11,878	12,359	12,586	12,751
CDC	3,956	3,996	4,198	4,161	4,150	4,504	4,416	4,710	5,027	5,132
NIH	12,691	13,415	13,662	13,108	12,547	12,725	13,250	13,204	13,779	14,133
ADAMHA	1,624	1,660	1,643	1,556	1,489	1,577	1,700	1,743	1,912	2,048
St. Elizabeths	[3,768]	[3,859]	[1,757]	--	--	--	--	--	--	--
HCPR	--	--	--	--	--	--	--	--	--	170
OASH	1,675	1,600	1,547	1,430	1,422	870	873	946	965	819
Total, PHS	42,904	43,011	43,350	42,413	41,095	40,652	41,577	42,541	44,307	45,461
HCFA	4,359	4,125	4,090	4,020	3,904	3,829	3,812	3,926	4,017	4,127
SSA	82,951	82,434	79,841	77,928	75,513	70,988	67,074	64,706	63,224	63,599
FSA	1,390	1,354	1,236	1,232	1,146	1,046	979	993	1,029	1,029
OHDS	1,392	1,313	1,268	1,166	1,080	1,014	1,001	969	1,000	1,000
OS										
GDM	3,716	3,685	3,223	2,742	2,733	2,656	2,579	2,629	2,649	2,623
OIG	1,229	1,408	1,360	1,307	1,225	1,218	1,240	1,331	1,415	1,415
OCR	487	477	437	397	377	368	344	326	325	325
PR	16	15	16	6	5	5	5	5	5	5
Total, OS	5,448	5,585	5,036	4,452	4,340	4,247	4,168	4,291	4,394	4,368
Total, HHS	138,444	137,822	134,821	131,211	127,078	121,776	118,611	117,426	117,971	119,584
OCA	36	34	31	32	29	20	20	19	22	22
St. Elizabeths	3,768	3,859	1,757	--	--	--	--	--	--	--
Grand, Total	142,248	141,715	136,609	131,243	127,107	121,796	118,631	117,445	117,993	119,606
Change from 1982										-22,642
% Change										-16%

GOALS AND OBJECTIVES

Mr. Natcher: The budget document indicates that the Department has three initiatives in the Management by Objectives System relating to health improvement, strengthening families, and enhancing Social Security Administration service. Describe what goals you have identified to meet these objectives and how they will be measured. When can we expect an initial progress report?

Secretary Sullivan: The following goals have been identified as supporting the three HHS objectives in the President's MBO system:

Objective I

To improve the health of the American people.

Goals supporting this objective:

Improve Access to Health Care
Continue Quality Biomedical Research and Improve Effectiveness of Medical Treatment
Enhance Health Promotion

Objective II

To strengthen families and assure family obligations

Goal supporting this objective:

Improve the strength of the American family by:

o providing Federal leadership in improving the adoption system

o providing Federal leadership in improving the foster care system

o implementing the Family Support Act JOBS program and related provisions

o enhancing child support enforcement implementing provisions in the Family Support Act

Objective III

To enhance the quality of services the Social Security Administration delivers to the public

Goal supporting this objective:

To enhance the quality of services the Social Security Administration delivers to the public by:

- o improving telephone access through reduction of busy signal rates

- o expanding the number of transactions that can be completed over the telephone

- o shortening telephone time required to complete transactions

- o improving claims processing

- o reducing the processing time and backlogs for appeals

- o improving service responsiveness through reduction of office waiting times

The Department is tracking accomplishment of these goals and is reporting results to OMB after each quarter. The most recent quarterly MBO update was submitted to OMB on February 9.

NATIVE HAWAIIANS

Mr. Natcher: Provide a table for 1990 and 1991 identifying HHS resources channeled to Native Hawaiians, either through programs specifically targeted to this population or through set-asides within more broadly defined programs.

Secretary Sullivan: The information is presented in the following table:

(Dollars in Millions)

Program	1990	1991
HRSA:		
Payments to Hawaii for treatment of Hansen's Disease	$3	$3
Native Hawaiian Health Care	1	1
Subtotal, HRSA	$4	$4
HDS:		
Aging Grants	1	2
Native Americans Programs:		
Native Hawaiians	1	1
Demonstration Revolving Loan Fund	1	0
Subtotal, HDS	$3	$3
Total	$7	$7

MINORITY TRAINING PROGRAMS

Mr. Natcher: Provide a table displaying funding for minority training programs throughout the Department for 1989-1991.

Secretary Sullivan: The following table displays HHS minority targeted training programs.

(Dollars in millions)

	1989	1990	1991
HRSA:			
Health Professions.....	$43	$43	$58
National Health Service Corps Scholarships & Loans.	--	--	55
Institutional Development...	--	--	12
Community-based Recruitment.	--	--	5
Subtotal, HRSA.....	$43	$43	$130
NIH:			
Access to Research Careers..	$9	$11	$13
High School Apprenticeship...	2	2	3
Minority Fellowships & Grants.	3	3	3
Subtotal, NIH.....	$14	$16	$19
ADAMHA:			
Access to Research Careers...	$1	$1	$1
Institutional Research Dev...	-	1	1
Minority Fellowships.....	3	3	2
Subtotal, ADAMHA.....	$4	$5	$4
Total, HHS.....	$61	$64	$153

PEDIATRIC AIDS RESOURCES

Mr. Natcher: Provide a table identifying HHS resources targeted to pediatric AIDS for 1989-1991.

Secretary Sullivan: The information is as follows:

HHS - PEDIATRIC AIDS EXPENDITURES
(Dollars in $000s)

	1989	1990	1991
PHS:			
HRSA:			
Pediatric AIDS Health Care Demonstrations..	$7,806	$14,803	$14,803
CDC:			
Pediatric AIDS Surveillance.....	$988	$1,318	$1,520
Perinatal Transmission Studies.....	1,976	2,500	3,520
Natural History Studies.....	1,383	2,500	3,325
Neonatal Seroprevalence Studies.....	14,033	14,049	14,100
Perinatal AIDS Prev. Demonstrations.....	6,305	7,342	21,993
Subtotal, CDC.....	$24,685	$27,709	$44,458
NIH:			
NCI.....	$3,940	$7,891	$10,200
NHLBI.....	1,630	4,182	5,060
NINCDS.....	1,131	1,393	1,491
NIAID.....	22,769	34,572	36,924
NICHD.....	18,045	22,500	24,500
DRR.....	7,561	3,141	3,296
NCNR.....	160	140	150
Subtotal, NIH.....	$55,236	$73,819	$81,621
ADAMHA:			
NIMH.....	$4,550	$5,400	$9,840
NIDA.....	3,700	3,800	3,900
Subtotal, ADAMHA....	$8,250	$9,200	$13,740
Total, PHS.....	$95,977	$125,531	$154,622
OHDS:			
Child Welfare Services Demonstrations.....	$2,200	$1,500	$7,500
Abandoned Infants Assistance.....	---	9,867	9,867
Total, OHDS.....	$2,200	$11,367	$17,367
TOTAL, HHS Discr. Pediatric AIDS.....	$98,177	$136,898	$171,989

MCKINNEY ACT

Mr. Natcher: Provide a table showing funding for programs authorized under the Stewart B. McKinney Act for 1989-1991, separately identifying any forward funding.

Secretary Sullivan: The following table shows the funds appropriated for the Department's McKinney Act Programs.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

McKinney Act Funding

(Dollars in Thousands)

	FY 1989 Actual	FY 1990 Approp.	FY 1991 Pres. Budget
ADAMHA:			
Mental Health Homeless Demonstrations	$4,594	$6,038	$6,006
Alcohol Community Demonstrations	4,545	16,378	9,043
Advanced Funding from FY 90	0	0	455
State Grants for Homeless/Mentally Ill	14,128	27,813	26,799
Advanced Funding from FY 90	0	0	6,904
Total Program Level, ADAMHA	$23,267	$50,229	$49,207
HRSA:			
Primary Care Grants	$14,820	$33,667	$33,667
Advanced Funding from FY 90	0	0	11,885
Total Program Level, HRSA	$14,820	$33,667	$45,552
FSA:			
Community Services for the Homeless	$18,918	$21,855	$33,959
Advanced Funding from FY 90	0	0	8,041
AFDC Transitional Family Housing	N/A	20,000	(to HUD)
Total Program Level, FSA	$18,918	$41,855	$42,000
Total, McKinney Act Programs	$57,005	$125,751	$136,759
Subtotal, Advanced Funding from FY 90	0	0	27,285

INFANT MORTALITY

Mr. Natcher: Provide the most recent available data on the U.S. infant mortality rate from 1980 to the present, displaying both total and race-specific data.

Secretary Sullivan: The information is as follows:

U.S. INFANT MORTALITY RATES
(per 1000 live births)

			Non-White	
Year	Total	White	All Non-White	Black
1980	12.6	11.0	19.1	21.4
1981	11.9	10.5	17.8	20.0
1982	11.5	10.1	17.3	19.6
1983	11.2	9.7	16.8	19.2
1984	10.8	9.4	16.1	18.4
1985	10.6	9.3	15.8	18.2
1986	10.4	8.9	15.7	18.0
1987	10.1	8.6	15.4	17.9
1988*	9.9	n/a	n/a	n/a

* Provisional.

UNAUTHORIZED PROGRAMS

Mr. Natcher: Provide a list of all programs funded in FY 1990 or proposed for funding in FY 1991 which are not presently authorized for FY 1991.

Secretary Sullivan: The list of programs lacking authorization follows:

Program	Request
Public Health Service:	
HRSA:	
National Health Service Corps:	
Field placements	$42,361
Recruitment	63,882
HUD Health Service Grants	35,000
Health Professions	
Institutional Development	12,000
Community Based Recruitment & Support	5,000
CDC:	
Immunization Grant Program	130,862
Tuberculosis Control Grants	8,334
Chronic & Environmental Disease Prevention	22,660
National Center for Health Statistics	48,128

NIH:	
National Cancer Institute*.....	1,658,266
National Heart, Lung & Blood Institute*.....	1,068,026
Fogarty International Center.....	16,355
National Library of Medicine (library assistance).....	13,191
National Research Service Awards:	
NCI.....	35,793
NHLBI.....	44,476
NIDR.....	5,893
NIDDKD.....	23,872
NINDS.....	13,016
NIAID.....	17,493
NIGMS.....	85,650
NICHHD.....	16,562
NEI.....	7,105
NIEHS.....	10,586
NIA.....	9,520
NIAMSD.....	6,742
NIDCD.....	3,123
DRR.....	2,493
NCNR.....	4,233
NCHGR.....	5,066

* Specific authorization lacking; general authorization can be used.*

ADAMHA:	
Community Support Program (Mental Health)	26,862
OASH:	
Adolescent Family Life.....	9,431
Family Planning.....	139,135
Family Support Administration:	
Low Income Home Energy Assistance.....	1,050,000
Office of Refugee Resettlement.....	368,822
Community Services Homeless Grants.....	42,000
Fiscal Assistance to Puerto Rico.....	825,000
Office of Human Development Services:	
Head Start.....	1,886,315
Child Development Scholarships.....	1,431
Dependent Care Planning & Development...	13,178
Developmentally Disabled.....	98,477

"BUILT-IN" INCREASES - PERSONNEL COSTS

Mr. Natcher: Provide a table that identifies the Department's FY 1991 "built-in" increases for personnel compensation and benefits costs by account. For each account, separately identify the amount and percentage increase over the 1990 base

for the following items: the January 1990 pay raise, the January 1991 pay raise, within grade/promotions/bonuses (combined), one additional day of pay, executive pay raise, and FERS. Increased pay costs should include associated benefit costs increases. Exclude FDA, IHS and accounts which do not fund personnel costs. Also provide a general description of each of the increases and the basis, method, or assumptions for computing the cost increases.

Secretary Sullivan: The attached table shows the impact of the "built-in" personnel and benefit increases contained in the 1991 budget submission. The individual items were calculated as follows:

Pay Raise: includes increasing the pay base for fourth quarter of the 3.6% January 1990 pay raise, plus the 3.5% January 1991 pay raise with 50% absorption by the OPDIVs, for three- quarters of the year.

Within Grades, Promotions & Bonuses: based upon historical data, inflated for the percent increase in the pay raise.

Extra Day: 1991 contains one extra day of pay compared to 1990. The calculation is a daily proration of the annualized cost of salary and benefits.

Executive Pay: based upon pay increase of between 18 and 25% with 50% absorption by the OPDIVs, for three-quarters of the year.

FERS: based upon historical data, which as of December 31, 1989 assumes that 25.7% percent of all Departmental employees participate, and inflated for the percent increase in the pay raise.

All Other: the footnotes attached to the table provide guidance as to the factors used in deriving those figures.

It should be noted that A number of OPDIVs included the cost of the Executive Pay Raise and FERS increases in the calculation of the 1991 Pay Raise.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Built-in Increases for Personnel and Benefit Costs

(Dollars in thousands)

(% over 1990 total Pay and Benefits)

	Pay Raise				Within Grades, Promotions & Bonuses		Extra Day		Executive Pay Raise		FERS		Other Costs			Total	
	1990 (annualized)		1991														
	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent		Amount	Percent
PHS																	
HRSA	$1,193	1.12%	$4,286	4.03%	$925	0.87%	$274	0.26%	a)	n.a.	$278	0.26%	$0	0.00%		$6,956	6.54%
CDC	$2,227	1.00%	$6,486	2.92%	$1,963	0.88%	$560	0.25%	a)	n.a.	$380	0.17%	$1,160	0.52%	b)	$12,776	5.75%
NIH																	
NCI	$1,120	0.87%	$3,735	2.90%	$714	0.55%	$494	0.38%	a)	n.a.	a)	n.a.	$22	3.36%	c)	$6,085	4.70%
NHLBI	402	0.89%	1,569	3.46%	717	1.58%	166	0.37%	a)	n.a.	a)	n.a.	9	4.46%	c)	2,863	6.31%
NIDR	154	0.91%	586	3.47%	175	1.04%	67	0.40%	a)	n.a.	a)	n.a.	633	3.73%	d)	1,615	9.53%
NIDDKD	452	1.33%	1,366	4.03%	647	1.91%	135	0.40%	a)	n.a.	a)	n.a.	5	3.25%	c)	2,605	7.72%
NINDS	448	1.30%	1,134	3.30%	521	1.51%	133	0.39%	a)	n.a.	a)	n.a.	5	3.09%	c)	2,241	6.49%
NIAID	412	0.95%	1,280	2.96%	528	1.22%	176	0.41%	a)	n.a.	a)	n.a.	7	3.27%	c)	2,403	5.53%
NIGMS	69	0.84%	281	3.44%	54	0.66%	29	0.35%	a)	n.a.	a)	n.a.	1	3.03%	e)	434	5.29%
NICHD	236	0.89%	958	3.61%	469	1.76%	101	0.38%	a)	n.a.	a)	n.a.	4	3.20%	c)	1,768	6.62%
NEI	164	1.47%	682	6.12%	142	1.27%	46	0.41%	a)	n.a.	a)	n.a.	3	5.38%	c)	1,037	9.26%
NIEHS	288	0.94%	940	3.08%	231	0.76%	115	0.38%	a)	n.a.	a)	n.a.	6	3.06%	c)	1,580	5.15%
NIA	230	1.20%	658	3.43%	541	2.82%	49	0.26%	a)	n.a.	a)	n.a.	3	3.00%	c)	1,481	7.69%
NIAMSD	89	1.37%	295	4.54%	77	1.19%	26	0.40%	a)	n.a.	a)	n.a.	1	4.76%	e)	488	7.49%
NIDCD	26	0.79%	203	6.14%	42	1.27%	14	0.42%	a)	n.a.	a)	n.a.	0	0.00%		285	8.62%
RR	44	1.02%	252	5.85%	55	1.28%	21	0.49%	a)	n.a.	a)	n.a.	2	9.09%	e)	374	8.64%
NCNR	16	0.85%	80	4.27%	21	1.12%	7	0.37%	a)	n.a.	a)	n.a.	0	0.00%		124	6.62%
NCHGR	3	0.21%	58	4.05%	16	1.12%	6	0.42%	a)	n.a.	a)	n.a.	0	0.00%		83	5.80%
FIC	34	1.10%	84	2.73%	23	0.75%	12	0.39%	a)	n.a.	a)	n.a.	0	0.00%		153	4.97%
NLM	230	0.97%	831	3.51%	316	1.33%	93	0.39%	a)	n.a.	a)	n.a.	6	3.26%	c)	1,476	6.18%
OD	251	0.89%	1,146	4.04%	427	1.51%	113	0.40%	a)	n.a.	a)	n.a.	257	0.90%	f)	2,194	7.69%
Subtotal, NIH	$4,668	0.99%	$16,138	3.43%	$5,716	1.21%	$1,803	0.38%	a)	n.a.	a)	n.a.	$964	2.02%		$29,289	6.20%
ADAMHA	$803	0.80%	$3,104	3.11%	$1,290	1.29%	$359	0.36%	a)	n.a.	$284	9.16%	$6,335	6.14%	g)	$12,175	11.45%
ADCPR	$67	0.74%	$378	4.15%	$90	0.99%	$24	0.26%	a)	n.a.	$15	6.28%	$0	0.00%		$574	5.65%
OASH	$207	1.01%	$826	4.04%	h) $286	1.40%	$81	0.40%	a)	n.a.	$51	9.01%	$0	0.00%		$1,451	6.91%
TOTAL, PHS	$9,165	0.99%	$31,218	3.36%	$10,270	1.11%	$3,101	0.33%	a)	n.a.	$1,008	0.30%	$8,459	2.27%		$63,221	6.74%

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Built-in Increases for Personnel and Benefit Costs

(Dollars in thousands)

(% over 1990 total Pay and Benefits)

	Pay Raise				Within Grades, Promotions & Bonuses		Extra Day		Executive Pay Raise		FERS		Other Costs		Total	
	1990 (annualized)		1991													
	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent
HCFA	$1,661	0.87%	$2,392	1.33%	$0	0.00%	$618	0.34%	a)	n.a.	a)	n.a.	$0	0.00%	$4,671	2.55%
SSA	$22,845	1.25%	$56,344	3.08%	$42,882	2.34%	i) $0	0.00%	a)	n.a.	a)	n.a.	$3,000	2.88%	j) $125,071	6.46%
FSA	$551	1.15%	$1,277	2.66%	$0	0.00%	$0	0.00%	a)	n.a.	a)	n.a.	$0	0.00%	$1,828	3.81%
HDS	$440	0.87%	$669	1.32%	$633	1.25%	$0	0.00%	$64	0.13%	$277	0.55%	$328	0.65%	k) $2,411	4.77%
OS																
GDM	$580	0.78%	$1,704	2.29%	$1,000	1.34%	$0	0.00%	$1,502	2.01%	a)	n.a.	0	0.00%	$4,786	6.42%
OIG	599	0.90%	982	1.48%	742	1.12%	0	0.00%	a)	n.a.	a)	n.a.	0	0.00%	$2,323	3.49%
OCR	149	0.90%	446	2.69%	189	1.14%	0	0.00%	a)	n.a.	a)	n.a.	0	0.00%	$784	4.73%
PR	10	2.67%	0	0.00%	0	0.00%	0	0.00%	a)	n.a.	a)	n.a.	0	0.00%	$10	2.67%
OCA	0	0.00%	49	4.85%	l) 0	0.00%	0	0.00%	a)	n.a.	a)	n.a.	0	0.00%	$49	4.85%
Total, OS	$1,338	0.85%	$3,181	2.00%	$1,931	1.22%	$0	0.00%	$1,502	2.01%	a)	n.a.	$0	0.00%	$7,952	5.00%
TOTAL, HHS	$35,900	1.12%	$95,081	2.97%	$55,716	1.88%	$3,719	0.34%	$1,566	1.25%	$1,285	0.34%	$11,787	0.00%	$205,054	6.19%

Notes:

a) Increase was calculated as a part of Pay Raise.

b) Annualization of new positions and Medicare and FICA increases.

c) Federal Employees Compensation Fund and Unemployment compensation increases.

d) Federal Employees Compensation Fund, Unemployment compensation increases, and annualization of new positions.

e) Federal Employees Compensation Fund increases.

f) Federal Employees Compensation Fund, Unemployment compensation increases, and annualization of 1989 AIDS FTE increase.

g) Annualization of new positions, Unemployment compensation, St. Elizabeth's workers compensation.

h) Includes Executive Pay Raise.

i) Includes FERS increases.

j) Federal contribution to employee health benefits increases.

k) Merit pay increases and cost for additional management interns and stay-in-school programs participants.

l) Includes salary benefits increase.

"BUILT-IN" INCREASES - NON-PERSONNEL COSTS

Mr. Natcher: Provide a table which identifies the Department's FY 1991 "built-in" increases for non-personnel costs by account. For each account, separately identify the amount and percentage increase over the 1990 base for the following items: service and supply fund, laboratory supplies, and centrally furnished services, FTS, and space rental. Exclude FDA, IHS, and accounts which do not fund these costs. Also provide a general description of each of the increases and the basis, method, or assumptions for computing the cost increases.

Secretary Sullivan: The attached table shows the impact of the "built-in" non-personnel increases contained in the 1991 budget submission. The individual items were calculated as follows:

Service and Supply Fund, Laboratory Supplies, and Centrally Furnished Services: based upon historical data, planned program expansions, and inflated for one-half of the OMB-supplied non-defense, non-pay deflator.

FTS: based upon historical data, adjusted for the impact of FTS 2000 (new phone system).

Rental Space: calculated based upon assumptions of 135 square feet per employee and the GSA-provided cost for government owned space, where appropriate, or the agencies projected cost of leased space.

Other Costs: the footnotes to the attached table provide guidance as to the factors used in deriving those figures.

Please note:

Space rental costs in some instances are charged against a service and supply fund or centrally supplied services and are therefore not reflected as a separate item within the calculations. Because the request specifically asks for information related to the "Service and Supply Fund", which refers to PHS, any cost increase in supplies for other OPDIVs was included in a separate category, "Other Costs".

Because this table and the preceding one are similar in nature, we have continued the lettering of the footnotes from the preceding table to this one in order to eliminate confusion. Thus the last footnote on the preceding table is l) and the first footnote on this table is m).

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Built-in Increases for Non-Personnel Costs

(Dollars in thousands)

(% Increase over 1990 Budget Baseline)

	Service and Supplies Fund		Laboratory Supplies		Centrally Furnished Services		FTS		Space Rental		Other Costs		Total	
	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent
PHS														
HRSA	$48	0.51%	$0	0.00%	$0	0.00%	$0	0.00%	m)	n.a.	$687	12.18% n)	$735	4.86%
CDC	$376	0.38%	$0	0.00%	$1,495	1.50% o)	$0	0.00%	$416	5.23%	$11,825	6.95% p)	$14,112	5.22%
NIH														
NCI	$1,034	3.30%	$4,717	3.92%	$8,364	7.00%	$59	3.15%	m)	n.a.	$0	n.a.	$14,174	5.19%
NHLBI	n.a.	0.00%	1,401	3.55%	2,600	5.32%	20	3.71%	m)	n.a.	0	n.a.	4,021	4.52%
NIDR	20	0.64%	415	3.29%	342	4.84%	6	2.44%	m)	n.a.	0	n.a.	783	3.36%
NIDDKD	42	0.27%	1,293	4.22%	1,025	4.14%	16	2.38%	m)	n.a.	0	n.a.	2,376	3.31%
NINDS	936	3.60%	n.a.	0.00%	2,154	9.29%	14	3.26%	m)	n.a.	0	n.a.	3,104	5.21%
NIAID	242	4.36%	2,166	3.36%	4,087	13.50%	18	3.63%	m)	n.a.	0	n.a.	6,513	6.49%
NIGMS	10	0.23%	320	3.34%	374	6.07%	4	4.35%	m)	n.a.	0	n.a.	708	3.52%
NICHD	409	3.50%	1,526	3.26%	838	3.58%	13	3.13%	m)	n.a.	0	n.a.	2,786	3.38%
NEI	120	3.67%	424	3.30%	625	7.24%	6	3.33%	m)	n.a.	0	n.a.	1,175	4.71%
NIEHS	n.a.	0.00%	1,338	3.38%	269	12.27%	1	2.86%	m)	n.a.	0	n.a.	1,608	3.85%
NIA	98	3.43%	459	2.72%	798	13.30%	5	3.97%	m)	n.a.	0	n.a.	1,360	5.26%
NIAMSD	n.a.	0.00%	123	2.37%	883	12.41%	2	3.85%	m)	n.a.	0	n.a.	1,008	8.15%
NIDCD	n.a.	0.00%	56	0.91%	103	9.26%	1	3.33%	m)	n.a.	0	n.a.	160	2.20%
RR	52	4.74%	91	2.68%	514	19.56%	2	2.27%	m)	n.a.	0	n.a.	659	9.14%
NCNR	2	1.60%	24	3.27%	197	48.40%	1	4.76%	m)	n.a.	0	n.a.	224	17.39%
NCHGR	0	0.00%	17	2.40%	n.a.	0.00%	0	0.00%	0	n.a.	0	n.a.	17	2.40%
FIC	59	25.43%	0	0.00%	93	11.63%	1	2.63%	m)	n.a.	167	9.18% q)	320	11.22%
NLM	n.a.	0.00%	0	0.00%	471	5.72%	8	3.39%	m)	n.a.	1,592	5.22% q)	2,071	5.32%
OD	72	3.56%	0	0.00%	n.a.	0.00%	7	3.52%	m)	n.a.	930	3.57% q)	1,009	3.57%
Subtotal, NIH	$3,096	2.88%	$14,370	3.51%	$23,737	7.41%	$184	3.19%	m)	n.a.	$2,689	4.61%	$44,076	4.84%
ADAMHA	$2,109	3.94%	$1,880	3.30%	$0	0.00%	$26	3.29%	$316	9.02%	$2,417	2.40% r)	$6,748	6.02%
ADCPR	$65	9.92%	$0	0.00%	$0	0.00%	$6	3.13%	$12	3.95%	$11	16.18% s)	$94	7.71%
OASH	$127	9.10%	$0	0.00%	$0	0.00%	$14	3.20%	$68	2.75%	$9	2.60%	$218	4.68%
TOTAL, PHS	$5,821	2.14%	$16,250	3.48%	$25,232	6.00%	$230	3.41%	$812	6.90%	$17,638	5.27%	$65,983	5.04%

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Built-in Increases for Non-Personnel Costs

(Dollars in thousands)

(% Increase over 1990 Budget Baseline)

	Service and Supplies Fund		Laboratory Supplies		Centrally Furnished Services		FTS		Space Rental		Other Costs		Total	
	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent	Amount	Percent
HCFA	$0	0.00%	$0	0.00%	$0	0.00%	$0	0.00%	$588	4.29%	$5,296	4.21% t)	$5,884	4.22%
SSA	$0	0.00%	$0	0.00%	$20,927	12.24% u)	$0	0.00%	$8,340	2.89%	$54,000	7.24% v)	$83,267	7.27%
FSA	$0	0.00%	$0	0.00%	$0	0.00%	$0	0.00%	$283	5.35%	$0	0.00%	$283	5.35%
HDS	$0	0.00%	$0	0.00%	$0	0.00%	$0	0.00%	$0	0.00%	$777	4.30% w)	$777	4.30%
OS														
GDM	$0	0.00%	$0	0.00%	$0	0.00%	$0	0.00%	$653	5.00%	$0	0.00%	$653	5.00%
OIG	0	0.00%	0	0.00%	0	0.00%	0	0.00%	180	4.20%	79	3.36% x)	259	5.36%
OCR	0	0.00%	0	0.00%	0	0.00%	0	0.00%	174	9.01%	0	0.00%	174	9.01%
PR	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	6	0.20%	6	0.20%
OCA	0	0.00%	0	0.00%	0	0.00%	0	0.00%	0	0.00%	31	3.77% y)	31	3.77%
Total, OS	$0	0.00%	$0	0.00%	$0	0.00%	$0	0.00%	$1,007	5.22%	$116	1.90%	$1,123	4.76%
TOTAL, HHS	$5,821	2.14%	$16,250	3.48%	$46,159	7.81%	$230	3.41%	$11,030	3.26%	$77,827	7.04%	$157,317	5.96%

Notes:

m) Space costs calculated as a part of Centrally Supplied Services, Service and Supply Fund or Other Costs.

n) Includes FTS and rental costs

o) Computer Center costs and Working Capital Fund

p) Utility and fuel increases, and contract and vaccine costs

q) Supplies, materials, and other mandatory program increases.

r) Working Capital Fund increases and restoration of program cuts used to absorb 1990 pay raise.

s) Working Capital Fund increases.

t) Postage increases, inflation, and sequester restoration.

u) ADP related cost increases.

v) Developmental Disability Service cost increases.

w) Travel, postage, telecommunications, printing, contract, supply and data processing equipment cost increases.

x) Working Capital Fund increases.

y) Inflation related increases.

NIH CONFLICTS-OF-INTEREST

Mr. Conte: At the end of last year, you surprised the biomedical research community with your decision to suspend NIH's proposed guidelines on potential conflicts-of-interest among researchers involved with NIH grants. You said at the time that you still intended to address the conflict-of-interest problem through the formal regulatory channels. What is the status of your conflict of interest plans?

Secretary Sullivan: On September 15, 1989, NIH proposed new guidelines to address potential conflicts-of-interest among extramural research projects supported by NIH. These guidelines were published in the "NIH Guide for Grants and Contracts". In general, the guidelines would prohibit NIH grantees, or their families, from having a financial interest in the results or potential products of their research.

On December 29, 1989, in light of widespread concern about the effects of the guidelines, I instructed the NIH to rescind the proposed guidelines. Instead, I requested that NIH prepare a set of options for addressing potential conflicts-of-interest which would ensure the integrity of NIH supported research without excessive or counterproductive regulatory impediments. I understand that NIH has begun work on these options, however, they have not as yet been presented to me.

Mr. Conte: When do you anticipate having the notice of proposed rule making published?

Secretary Sullivan: Any changes made to grantee eligibility with respect to conflict of interest will be implemented through the formal Federal regulatory process. This process will include the issuance of a Notice of Proposed Rulemaking (NPRM), a public comment period, and a publication of the Final Rule with an additional public comment period. At this time we have set no precise schedule for publication of the conflict-of-interest rule.

HUMAN GENOME PROJECT

Mr. Conte: The Human Genome Initiative is now off and running. The budget request adds $48 million for a total of $108 million for FY91. I hear that the cost of sequencing each pair of DNA has fallen from $5 to around $2. Since there are 3

billion base pairs in the human genome, the potential cost to complete the sequencing is enormous. What are the prospects for lowering the cost of sequencing?

Secretary Sullivan: Given the extremely fast pace biomedical science and technology is progressing we are optimistic that new, lower cost methods of sequencing will be available in the future. We still estimate that a significant Federal investment by NIH and DOE will be necessary for the next several years to meet the task at hand.

Mr. Conte: Are there new techniques in the pipeline that would dramatically lower costs?

Secretary Sullivan: As indicated in the five-year plan which was just completed jointly by NIH and the Department of Energy, we will devote a substantial amount of resources and effort over the next five years to developing more effective and efficient technologies for gene mapping. While we certainly believe that tools such as scanning tunneling microscopy and mass spectrometry will be helpful in our efforts to map the human genome, it is also quite possible that the ultimate sequencing technology is a method has yet to be developed.

Mr. Conte: Is the polymerase chain reaction a potential tool that would lower the sequencing costs?

Secretary Sullivan: Polymerase chain reaction is one of the tools that has eased the way toward the initial stages in the construction of physical maps of large, non-human genomes. While the current cost of sequencing a base pair ranges from $2 to $3, we believe the cost needs to be lowered below $0.50 before the project will become financially feasible. The maximum reduction in cost of current sequencing technology will come from the creation of a fully automated assembly line for rapid DNA sequencing. Computers which automatically perform the basic steps of identifying the order of the base pairs are available.

DRUG ABUSE MEDICATION DEVELOPMENT

Mr. Conte: How much money is in the ADAMHA budget for the Medication Development Program for FY 1991?

Secretary Sullivan: The 1991 budget includes $40 million for National Institute on Drug Abuse's medication development program.

Mr. Conte: How many medications are currently being evaluated?

Secretary Sullivan: The National Institute on Drug Abuse's medication development program, for which $40 million is included in 1991 budget, is currently investigating 25 different potential medications.

Mr. Conte: What is the average cost of developing a medication?

Secretary Sullivan: The National Institute on Drug Abuse expects the average cost of developing a medication for drug abuse treatment to be similar to the industry-wide cost of developing a medication ($125 million). Aggregate data indicates that developing a medication takes approximately 10 years.

Mr. Conte: What are the key research opportunities for the program?

Secretary Sullivan: Recently, our research has provided us with new research opportunities. Research has provided knowledge on the pleasure center of the brain, on the receptors in the brain, and more about the compounds and their effects on the brain. One significant breakthrough in understanding the addictive properties of cocaine occurred 2 years ago at National Institute on Drug Abuse's (NIDA) Addiction Research Center. Scientists identified the molecule in the brain most likely to be responsible for mediating the rewarding properties of cocaine. This molecule is found on a pumping mechanism that is used by nerve cells to inactivate the dopamine that is released during the normal course of neuronal communication. One group of dopamine-containing neurons mediates the subjective feelings of pleasure. Because the consumption of cocaine blocks the inactivation, or reuptake, of dopamine, normal feelings of pleasure are intensified.

ADAMHA RESEARCH GRANTS

Mr. Conte: At ADAMHA, the President's budget provides for $494 million for research project grants, an increase of $42 million. Yet the number of new and competing grants will fall throughout ADAMHA. The number of new grants at NIMH will be cut by 31%. At the Alcohol institute, the total number of new grants would be slashed by nearly 60% -- from 190 to 80. And even with all our efforts in fighting drug abuse -- we're pouring billions into the budget -- NIDA will be seeing a 12% cut in new

awards (from 278 to 245). It seems to me that if we are going to make any headway in fighting drug abuse and in helping those with alcoholism, mental illness, we ought to be increasing the number of new projects. Doctor, what is going on here? Are the rising costs and the growing length of continuing grants part of the problem -- squeezing out funds for new grants?

Secretary Sullivan: I believe the Alcohol, Drug Abuse and Mental Health's (ADAMHA) research portfolio is of excellent quality and I am committed to continuing the quality of this portfolio in FY 1991 and beyond. It is important to provide the research community stable funding over time. Fluctuation in the total amount of dollars available often have a destabilizing effect on the research community. In FY 1990, all three ADAMHA research institutes received large increases in the number of research project grants. These projects, by necessity, will consume a large portion of the funding available for research in FY 1991. In total, the number of non-AIDS research project grants will increase by 61 compared to 1990 and 358 compared to 1989. This represents a record high level of support for total ADAMHA research project grants.

DRUG TREATMENT SLOTS

Mr. Conte: This budget discontinues funding for the drug waiting list program which received $64 million for FY90. How will people being helped by this program be served in the future?

Secretary Sullivan: In 1990, Congress appropriated $64 million on the condition that additional authorization be passed. Under current law only $25 million of the $64 million may be spent on Waiting List Reduction Grants. In 1988, Congress provided a program authorized at $100 million for Waiting List Reduction Grants. $75 million was appropriated in 1989, leaving $25 million left for appropriation in 1990. In addition, there is no authorization for this program in FY 1991.

While no funds are requested for this program in FY 1991, treatment slots created through this program should be maintained. One condition of receiving a Waiting List Reduction Grant is the grantee must guarantee that services provided by these grants will be continued once Federal funding is no longer available.

Mr. Conte: Are there enough treatment slots available to those who need them?

Secretary Sullivan: The Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) is committed to providing quality treatment to those persons suffering from a drug addiction. ADAMHA will fund a total of 108,000 treatment slots in 1991. This is an increase of 4,000 above the 1990 level. A slot can treat more than one person a year and the average number of persons per slot is approximately 2.5 per year.

The Federal government is only one source of drug treatment funding. State and local governments, third party insurers, and private funding sources are all important players in providing treatment. In fact, the National Drug Control Strategy II states that according to the 1987 National Drug and Alcoholism Treatment Unit Survey (NDATUS) funding for treatment is provided by: State and local governments (33 percent), the Federal government (23 percent), third party insurers (27 percent), and private individuals and charities (17 percent).

Mr. Conte: Isn't there a problem in the distribution and usage of various treatment centers?

Secretary Sullivan: The newly created Office for Treatment Improvement (OTI), headed by Dr. Beny Primm, will focus its efforts on communities which need special assistance, such as cities and rural areas.

In 1990 and in our 1991 budget we are increasing our data collection activities on drug treatment. We expect this information to help us determine more effective ways of assisting States and communities in providing quality treatment, as well as identifying and resolving any potential allocation problems which may exist.

MEDICARE FUNDING

Mr. Conte: Dr. Sullivan, one of my big concerns is the $5.5 billion cut in Medicare. Year after year Congress has had to confront higher health care costs for our senior citizens. It's been a top concern of mine for many years. It's unfair to single out this program as a target for the budget axe. We must assure our seniors that high quality hospital and physician services will be available. What is the rationale behind these cuts?

Secretary Sullivan: As you know, Medicare costs are one of the fastest growing parts of the Federal budget. In about 15 years, current projections indicate that spending for Medicare will exceed spending for either national defense or Social Security. If spending for current Medicare benefits is not brought under control, it will squeeze out the health care dollars needed to meet the other urgent health needs facing our nation. But let me emphasize that our proposed cuts are not just driven by budgetary pressures. We believe that they are reasonable and equitable and should be undertaken even in the absence of that pressure.

In addition to stressing managed care as means of assuring high quality, cost-effective health care delivery, our FY 1991 proposals include a number of items that are intended to anticipate and facilitate movement to the major physician payment reform enacted by Congress last year. We are also addressing a number of areas in which there is clearly excessive or duplicative payments. Our obligation to be a wise and prudent custodian of the public's money requires these cuts.

Mr. Conte: What assurances can you give our senior citizens that essential services won't be scaled back?

Secretary Sullivan: Our proposals will not result in any reduction in essential services. In fact, we believe that they will enhance service to our senior citizens. The managed care initiatives are designed to encourage more comprehensive care. The high levels of spending for research and peer review will help to assure that the care that is delivered is effective and appropriate. The physician payment proposals will help smooth the transition to the relative value scale in 1992, which in turn is expected to shift treatment more to primary care, to prevention rather than correction.

AIDS - LOW INCOME AZT DRUG ASSISTANCE PROGRAM

Mr. Conte: The cost of AZT, the drug that prolongs the lives of HIV infected people, is tremendous. Even with the minor price decreases by the manufacturers and the lowering of the necessary daily dosage, the annual cost of AZT still runs into thousands of dollars. Yet, this budget proposes to eliminate assistance to low-income AIDS patients who desperately need AZT to keep alive. The FY 1990 level is about $30 million. If the program is ended, are there other assistance programs available to help pay the high cost of AIDS-related drugs?

Secretary Sullivan: Where the patients qualify based on need, the Federal Medicaid and Medicare programs are involved in paying for AIDS treatment. About 40% of all AIDS patients have their care paid for through Medicaid. The estimated $870 million in Federal Medicaid payments in 1991, plus the approximately $870 million in State matching funds, are expected to account for nearly 25% of total national AIDS medical costs. Since many private insurers and all State Medicaid programs now include coverage for some HIV treatment drugs, such as AZT, we believe the categorical funds for AIDS drug reimbursement have served their transitional purpose and are no longer required.

We are also concerned that we avoid seeking solutions to a health care problem that foster a separate, or parallel, disease-specific approach that is not integrated with existing services and financing systems. Such approaches can be inefficient, unmanageable, and wasteful. If AIDS has highlighted the need for any health care reforms, we believe they should be dealt with in the context of the entire health care system, and not on a piecemeal, disease-by-disease basis. This is one of the major issues that is being looked at by both the Department's Health Policy Task Force Steering Committee, being chaired by Under Secretary Constance Horner, and the Steelman and Pepper Commissions.

CDC INFECTIOUS DISEASES

Mr. Conte: At the CDC, funding for AIDS will increase by $66 million (15%) to over a half a billion dollars. At the same time, however, the budget proposes to provide level funding for infectious and sexually-transmitted diseases. We've seen a major outbreak in measles this year -- and Lyme disease continues to spread across the country. While it's important to maintain growth in AIDS funding at CDC, it's also important to keep pace with other infectious diseases that strike millions of Americans. Doctor, how will CDC be able to keep up with the rising incidence of infectious diseases like Lyme disease with this budget?

Secretary Sullivan: The 1991 budget request for CDC of $1,172 million represents an overall increase of 7%, or +$87 million over 1990. This includes a 15% increase for AIDS and a 2% increase for non-AIDS activities. Even though more people are currently affected by other infectious and chronic diseases, we believe our extraordinary efforts to fight AIDS and HIV infection are still

warranted and command a higher priority at this time. This is the case for several reasons. AIDS is an infectious disease, which, if not kept in check now, could grow into an even larger epidemic. AIDS can lie hidden for years, without symptoms, in those who are infected, and the virus can be transmitted during this time. Most importantly, AIDS is still virtually fatal; available AIDS drugs, such as AZT and aerosolized pentamidine, only delay the progression of the disease, not cure it. AIDS, unlike many other causes of death, primarily strikes young Americans in their prime. AIDS is also now the ninth leading cause of death among children 1 to 4 years of age, and the seventh in young people between the ages of 15 and 24. Racial and ethnic minority populations are increasingly disproportionately affected by the epidemic, including about 43% of all reported cases to date. We also believe that finding the keys to unlock the AIDS mystery will help many others with other diseases. We are already beginning to see spin-offs from our AIDS work into other areas such as immunology, cancer retroviruses, and minority health education.

Furthermore, while the request for CDC's Sexually Transmitted Disease (STD) budget did not receive a further increase in 1991, the successful implementation of information and education programs to prevent the spread of AIDS/HIV by changing sexual and other high-risk behaviors, for which CDC's 1991 budget has been increased by about $66 million, should have a positive effect on reducing all STDs. More directly, CDC is currently working to ensure that all State and local AIDS prevention activities also support syphilis control efforts. In addition, it appears that the rise in crack-cocaine usage and the practice of exchanging sex for crack is also a cause for rising STD cases. Our major push to expand anti-drug abuse prevention and treatment efforts should therefore also contribute to controlling STDs. Throughout the PHS, funds for these anti-drug abuse activities are proposed to be increased in 1991 by $162 million, or +13% over 1990, and by $629 million, or +85% over 1989 levels.

With respect to Lyme's Disease, the 1991 budget request maintains the $2 million increase Congress added in 1990 to CDC's budget. In addition to these CDC monies, the National Institutes of Health is expected to spend about $6.4 million on research related to Lyme's Disease in 1991, an increase of $475,000 over 1990.

CDC DISABILITIES PREVENTION

Mr. Conte: I'm pleased to see that CDC has been making progress in disability prevention. Prevention of primary and secondary disabilities among low income and minority populations is especially important. The budget proposes $4.5 million for the program, level funding. I'll be co-sponsoring a bill with Henry Waxman to expand disability prevention grants so that more states can start their own programs with assistance from CDC. It would authorize $10 million for FY 1991. If we provided full authorization for disability prevention, how could CDC expand this program?

Secretary Sullivan: The 1991 budget includes $4.4 million for CDC activities related to disability prevention. This maintains the expanded program level resulting from the 1990 Congressional appropriation, and represents a 16% increase over 1989. These funds are being used to enhance the capacity of States for coordinating disabilities prevention programs and constructing surveillance systems for birth defects and developmental disabilities; to provide technical assistance to States and local communities in establishing networks and implementing such programs; and to conduct training and workshops for States for technology transfer. If additional funds were included above the President's budget request, we would expect that CDC would expand current activities.

It should also be noted that interest has been raised about creating a new Center for Rehabilitative Medicine at NIH, probably as part of an existing Institute.

Mr. Conte: How many more states would be included?

Secretary Sullivan: The $4.4 million available for 1990 currently supports disabilities prevention projects in nine States.

LEAD POISONING PREVENTION

Mr. Conte. Doctor, as you know, lead poisoning takes its toll upon poor and disadvantaged children. Pittsfield in my district has been having problems with homes that still have lead-based paint. The budget provides level funding for CDC's lead prevention program. Doctor, isn't lead prevention an important public health priority for disadvantaged and minority children?

Secretary Sullivan: Preventing lead poisoning is an important public health priority, especially for disadvantaged and minority children. I have even suggested to Secretary Jack Kemp of the Department of Housing and Urban Development (HUD) that we meet to explore ways in which HHS and HUD can work together to reduce this public health hazard, especially in public housing units.

Specifically within our Department, the 1991 budget request for CDC maintains the $3.9 million appropriated in 1990 for grants to States for childhood lead poisoning prevention activities, which includes screenings and medical referrals. In addition, CDC continues to provide technical assistance to the States on operating childhood lead poisoning screening and prevention programs, and on improving the performance of blood lead laboratory diagnosis.

Furthermore, funds from the HRSA Maternal and Child Health (MCH) Block Grant are also available to States to use for lead poisoning prevention. We are requesting that, in total, the MCH block grant be funded at $554 million in 1991, the same level as in 1990 and an increase of $180 million, or +48% over 1982. Because of limited block grant reporting requirements, we do not know exactly what the States are spending in the area of lead poisoning prevention. However, the information we do have indicates mixed impacts: several cities and States have significantly increased the number of children screened under the block grant, while others decreased their levels of lead screening program support.

NIH is also supporting several research projects studying the health effects of low levels of lead exposure in pregnant women, infants, and young children. For example, the National Institute of Environmental Health Sciences (NIEHS) is conducting basic research on how adverse health effects from lead exposure occur; developing tests to measure exposure before adverse effects take place; and developing improved treatment strategies, such as better chelation methods. The National Institute of Child Health and Human Development (NICHD) is studying the effects of prenatal transmission of lead through the umbilical cord and tooth lead levels on subsequent childhood behavior and learning abilities. Another study is examining the effects of low level lead exposure on hearing abnormalities.

SSA SERVICE IMPROVEMENTS

Mr. Conte: There have been service problems related to the staffing levels at SSA. Its absolutely imperative that we deliver the services that eligible people deserve. The budget includes $330 million more for SSA. What service improvements can we expect in the coming year, and in future years, from SSA?

Secretary Sullivan: In FY 1991 SSA is planning no major new service initiatives. However, we expect to improve existing services such as the "800" number. By FY 1991, we will have a year's experience on the "800" number and will be able to deal more effectively with cyclical call volumes and higher than anticipated telephone traffic. Also, teleservice representatives hired in FY 1990 will be more experienced thus providing better service to the public. Likewise, SSA will continue its high quality service delivery in face-to-face interviews in a district office setting.

MEDICAL TREATMENT EFFECTIVENESS PROGRAM

Mr. Conte: Secretary Sullivan, last year Chairman Natcher and I worked with you to get the Medical Treatment Effectiveness program off to a flying start. I see that the budget provides $11 million. Who decides which medical treatments get evaluated?

Secretary Sullivan: The 1991 budget request of $49 million provides an increase of $11 million for the Medical Treatment Effectiveness program over the level available in 1990. Decisions regarding which medical treatments get evaluated will be made based on recommendations of the Advisory Council on Health Care Policy, Research and Evaluation; interagency consultation within the Department; guidance provided by patient outcomes research teams with the expertise and perspectives of community and academic physicians; and to some extent will be investigator initiated.

Mr. Conte: How is that decision made?

Secretary Sullivan: Factors considered when making these decisions will include the number of individuals to be benefitted, the extent of uncertainty with respect to the use of a procedure or related outcome, the level of health expenditure and the availability of data. Also, priorities for research will reflect the needs of the Medicare program.

Mr. Conte: What are some of the new projects we might expect in the coming year from the effectiveness program?

Secretary Sullivan: In 1990 and 1991, we plan to study practice pattern variations involving the treatment of low back pain, heart attacks, cataracts, knee replacement, prostate gland enlargement, hip fracture and replacement, diabetes, cerebral vascular disease, pneumonia, congestive heart failure, colon cancer, biliary tract disease, cholecystectomy, ischemic heart disease, hysterectomy, and osteoarthritis.

JOBS PROGRAM

Mr. Conte: The budget proposes to add $557 million in new budget authority for the JOBS program, for a total of $1 billion. I support giving people the means to help themselves to better jobs and livelihoods. How are the States' allocations of JOBS funding determined.

Secretary Sullivan: The Family Support Act of 1988, P.L. 100-485, specifies both the maximum amount of JOBS funds available to all States in each year, and a formula by which JOBS funds are to be allocated among the States. Under this statutory formula, determining a State's allocation is a two step process. First, each State receives an amount equal to what it received in FY 1987 under the Work Incentives (WIN) program. Total funding of $126 million was provided for all States in FY 1987 for the WIN program. Secondly, the remaining funds, up to the cap for all States, are allocated to each State based on the State's share of the average monthly number of adult AFDC recipients in the preceding year relative to the total average monthly number of adult AFDC recipients in all States during the preceding year.

PEDIATRIC KIDNEY DISEASE

Mr. Conte: What can NIH do to improve research on Pediatric Kidney Diseases?

Secretary Sullivan: The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has primary responsible within NIH for research on kidney and urologic diseases. With a goal of reducing the incidence of kidney disease, especially those afflictions which lead to end stage renal disease, NIDDK research will further explore basic

mechanisms of renal function, continue evaluating the effect of diet on kidney function, and study the effects of hormones, diuretics and other drugs and toxins on kidney metabolism.

For those patients with advanced kidney disease such as end stage renal disease, NIDDK continues to explore improvements in dialysis technology and immunosuppressive medications necessary for successful kidney transplantation.

Finally, through its research training program, NIDDK will continue to encourage young investigators to chose careers in nephrology.

Mr. Conte: The budget proposal adds $24 million more for NIDDK. Is there enough to develop a "Centers of Excellence" program for pediatric nephrology?

Secretary Sullivan: In 1991, NIDDK will spend approximately $98 million to support basic and clinical studies on kidney diseases. Given the wide range of program responsibilities of the NIDDK, the 1991 budget plan does not call for development of a centers of excellence in pediatric nephrology. Nonetheless, we will use the additional funds requested to intensify research and training efforts in this field.

Mr. Conte: Would you work with NIH to see what we can do to improve research in pediatric nephrology?

Secretary Sullivan: Yes, I will work with NIH to see what improvements can be made within the funds available to the National Institute of Diabetes and Digestive and Kidney Diseases.

REFUGEE ASSISTANCE

Mr. Obey: What percentage of refugee assistance program cost will be shifted to the States in FY 1991?

Secretary Sullivan: States would have the same costs they have in FY 1990. The subsidy of State shares of Medicaid and AFDC costs would continue for four months after a refugee enters the United States. Refugees will continue to receive AFDC and Medicaid benefits as long as they are eligible, like other U.S. citizens.

Mr. Obey: What are the costs to be transferred to the States?

Secretary Sullivan: States' costs would not increase in FY 1991. The Federal Government pays 100% for a refugees' initial stay in this country for categorically eligible refugees and provides special cash and medical assistance to non-categorically eligible refugees for a 12 month period. Following this period, the Federal government continues to pay the existing matching rate, now averaging at 55%, for eligible benefit recipients.

Mr. Obey: The Wilson/Fish amendment to the Immigration and Nationality Act has been in effect since 1985. Yet as I understand it, only two States, California and Washington have been awarded grants. Can you explain this please?

Secretary Sullivan: California and Oregon, not Washington, have been awarded grants for the Fish/Wilson demonstration projects. No other States have applied. These demonstrations also permit States to transfer a portion of their Refugee Resettlement Assistance funds to private groups to facilitate refugee integration into the mainstream of employment and self-sufficiency; however, no State has chosen to transfer such funds.

Mr. Obey: I note that funding of employment services will be targeted to refugees who will be in this country for 3 years or less. Yet many States have high numbers of time expired refugees who remain dependent on public assistance. States like Wisconsin have highly successful employment programs for refugees, and many of the refugees who have been removed from public assistance through these programs have been in the country for longer than 36 months. Doesn't the targeting of these funds to time eligible refugees, in effect, pass on additional program costs to the States?

Secretary Sullivan: The employment services formula is based on a three-year population. However, any refugee is eligible for these services, regardless of how long they have been in the country. Costs for additional refugees can be met through JOBS, JTPA, Food Stamps, and Employment and Training programs.

LOW INCOME HOME ENERGY ASSISTANCE PROGRAM

Mr. Obey: LP and oil price increases since 1985 have significantly outstripped the average increase in wages. As a result, working people are paying a higher percentage of their income for home heating fuel. In many counties in the 7th district of Wisconsin, like in Portage County, non-welfare low income household participation in the program has increased dramatically since 1985 because more working poor people can't pay their entire fuel bill on their income. What percentage of LIHEAP participant households are working poor?

Secretary Sullivan: Information we receive from the Department of Energy indicates fuel oil prices for the FY 1989-1990 heating season, including the short-term abnormalities in December and January, will be 3 percent lower than in 1985. While wages and salaries increased 17 percent between March 1985 and September 1989, the Department of Energy projects that fuel oil prices will be 13 percent lower in the 1990-1991 season than in 1985. I also understand that only one-third of the families in Wisconsin use either LP or oil; most use natural gas.

Mr. Obey: By cutting LIHEAP, aren't we reducing yet another strategy for keeping working poor households in their own homes?

Secretary Sullivan: Department of Energy and Bureau Labor Statistics information suggest the answer to your question is no.

Mr. Obey: As I understand it, AFDC households represent less than 40% of all LIHEAP households. And most working poor are not eligible for most other programs like emergency assistance for AFDC for SSI recipients. In addition, FEMA vouchers are not available in most communities and eligibility for those are set by local boards who may or may not use them for fuel assistance needs when there are so many competing needs. How can the Administration claim that many households have other options available to them so LIHEAP isn't as important as it used to be?

Secretary Sullivan: We have suggested legislation that would increase the ability of States to concentrate LIHEAP on those not receiving energy assistance from other sources.

Mr. Obey: I also understand that most States do not index their AFDC or SSI payments and the minimum wage is not indexed. The only major benefit program which is indexed is social security. What is even worse, is that the Social Security tax has increased since 1980, more than offsetting the earned income credits most households receive, resulting in a net loss of income for many working poor households. How can the Administration, therefore, claim that most LIHEAP recipients are receiving benefits that are indexed for increases in the cost of living?

Secretary Sullivan: Social Security and Federal SSI benefits, the most important income sources for the elderly, are indexed for inflation. It is also our understanding that Wisconsin provides fuel assistance funding through the AFDC Emergency Assistance program. This is one of the eleven States that make such support available. All States have the option of using AFDC funds for energy assistance for AFDC families.

Mr. Obey: Is the percentage of income spent by the average low income household on home heating increasing or decreasing?

Secretary Sullivan: The percentage of income spent by low-income households on home heating has decreased from 4.2% in 1987 to 3.9% in 1988.

Mr. Obey: Is this trend expected to continue?

Secretary Sullivan: Yes, we expect that trend to continue.

Mr. Obey: What percentage of the average low income family is spent on home heating?

Secretary Sullivan: In FY 1988, the average expenditure for low-income households for home heating was $343 or 3.9% of the average household income.

Mr. Obey: If a family making $30,000 had to spend $4,200 for home heating, what do you think the public reaction would be?

Secretary Sullivan: We would obviously note that the example you give indicates that the family spends 7 to 8 times as much on heat as the average family in the Northeast, which has the highest heating costs of any census region.

Mr. Obey: The Wisconsin Division of State Energy reports that after a three year lull, home heating costs are back on the rise. The average low income family will spend a higher percentage of income on heating costs in 1990 than in 1985. Given that people are spending more, how can you justify cutting assistance?

Secretary Sullivan: While the average low-income family in Wisconsin may be spending more on heating costs this year than in 1985, for the nation as a whole, the percent of income that low-income households spend on home heating has decreased.

Mr. Obey: Wouldn't this cause undue hardship on low income consumers like those in Wisconsin who use unregulated fuels (LP and oil) which are much more market sensitive?

Secretary Sullivan: As I noted before, Census data indicate that only a third of Wisconsin residents use these fuels, with almost two-thirds using utility gas or electricity, which are regulated. LIHEAP's block grant nature gives Wisconsin the flexibility to target benefits on fuel oil and bottled gas users if their costs are higher than for families depending on regulated utilities.

HEAD START

Mr. Obey: A 1988 study by the American Council on Youth and Families revealed that 47% of Head Start teachers had salaries of $10,000 per year or less. Last year, in recognition of the serious problems in staff recruitment and retention of employees caused by these low salaries, we directed that a portion of the FY 1990 appropriation ($50 million) be used to begin to address this problem. What portion of the Administration's FY 1991 budget request would be used to address the staffing problems caused by low salaries of Head Start employees?

Secretary Sullivan: The FY 1991 budget continues the $50 million staff salary increase initiated by the Congress.

Mr. Obey: Do you have any concern that we might be focusing our efforts on expanding participation for children, but at the same time paying inadequate attention to the quality of the service these kids are getting?

Secretary Sullivan: Although expanding enrollment by 180,000 in one year will take a concentrated effort on the part of all persons working

with Head Start programs, every effort will be made to ensure that the additional children will be served without detracting from the quality and standards that we have come to expect from the Head Start program.

Mr. Obey: How can we expect to attract good people to the program if they can't make a decent living, Mr. Secretary? What specifically does the Administration intend to do about this problem?

Secretary Sullivan: The Administration intends to continue the $50 million increase first made available in FY 1990 for Head Start salary increases. This provided on average a 5.4% increase to Head Start staff. In addition, Head Start teachers received a 5.2 percent increase in FY 1988 and a 4.2 percent increase in FY 1987 for salaries and fringe benefits.

Mr. Obey: As I understand it, while current Head Start legislation and regulations enable Head Start programs to enroll children between the ages of 3-5 years, the President's proposal would expand enrollment by up to "180,000 four-year olds". Is it the intent of the Administration to provide Head Start expansion only for services to 4 year olds? Does the Administration have plans to actually prohibit future enrollment of 3 year olds, or to limit service to only one year?

Secretary Sullivan: The President's goal for Head Start is to provide one year of participation for all eligible children, preferably in the year before they enter kindergarten. Since all 50 States now provide public school kindergarten, primarily for 5-year olds, the greatest need, and the most potential benefit to be derived, is in serving four-year olds. The long-term goal, then, is to allow at least one year of Head Start to every disadvantaged four-year old in the nation. There are no plans, however, to prohibit future enrollment of 3 year olds, or to limit services to only one year.

Mr. Obey: The Head Start Act (section 638) provides that the Head Start program focus "primarily on children from low-income families who have not reached the age of compulsory school attendance..." Given this definition, how many children are eligible for Head Start services, and what percentage of <u>all</u> legally eligible children do you project to serve in FY 1991?

Secretary Sullivan: Although Head Start's legislation allows the program to serve children between birth and the age of compulsory school attendance, Head Start's primary focus has always been on serving 3-5 year old children (97% of current

enrollment are between 3-5 years old). Currently there are an estimated 2,475,000 low income three, four and five year olds. The 1991 President's budget request will enable Head Start to serve 622,000 of these children, or 25%. The remaining 66,000 children being served by Head Start are either less than three years of age, or from families with incomes above the poverty line.

However, it is estimated that all but a small portion of five year olds are enrolled in Kindergarten and, consequently, five year olds should not be considered as part of Head Start's target population. Thus Head Start considers its primary population as low-income three and four year olds. In FY 1991, there will be an estimated 1,650,000 low-income three and four year olds. The President's budget request would allow Head Start to serve 588,000 of these children, or 35.6% of the low-income three and four year old population. The remaining 80,000 children being served by Head Start in FY 1991 will be under three years of age, over four years of age, or from families with incomes above the poverty line.

RESEARCH FUNDING

Mr. Roybal: While federal funded research for Alzheimer's Disease totals about $135 million annually, funding for heart disease, AIDS and cancer total between $600 million and $1.5 billion annually. How does the Administration propose to rectify this imbalance?

Secretary Sullivan: Research on Alzheimer's Disease remains a top priority for both the National Institute on Aging and the National Institute on Mental Health. With this focus, we are making progress on discovering the causes of, and treatment for, Alzheimer's Disease.

The President's Budget request for the National Institutes of Health and the Alcohol, Drug Abuse and Mental Health Administration includes a total of $152 million for research on Alzheimer's Disease. This represents an increase of 4.2 percent over 1990 and 18.2 percent over 1989 levels. As a point of comparison, the 1991 requests for the National Cancer Institute and the National Heart, Lung and Blood Institute represent increases of 3.7 percent.

HEALTH CARE PROVISION

Mr. Roybal: Because many years have passed since we fully reviewed health care problems in our central cities, what specific steps is the Department taking to assess health care accessibility, affordability, and quality in our central cities and what actions should we take to address the problems we already know about?

Secretary Sullivan: As you may know, access to health care for all of our citizens is one of my highest priorities. Health care providers in our central cities are currently under siege in the war on drugs, are faced with the high costs associated with providing care to those with HIV/AIDS, are attempting to meet the challenge of caring for infants born with the inheritance of addiction, and are daily making decisions which force them to ration care as they confront the chronic dilemma of providing uncompensated care while jeopardizing the solvency of their health care organizations.

In terms of assessing the accessibility, affordability, and quality of health care in our central cities, I can safely say that we are continually evaluating our nation's health care delivery system through both the Office of Research and Demonstrations in the Health Care Financing

Administration and the Agency for Health Care Policy and Research in the Public Health Service. I have also established task forces which are presently studying the problems of the medically uninsured and access to health care for pregnant women.

Our 1991 budget proposal includes $3.4 billion to continue efforts to confront the toll of drugs and HIV/AIDS on our health care system and, in addition, includes several new initiatives which are intended to increase access to care for some of our most vulnerable citizens. In 1991, we propose a new $117 million initiative to improve the health status of minorities by fostering access to health care through increasing the number of minority heath faculty, providers, and minority health professionals in underserved areas, and providing readily available care in close proximity to public housing. The budget for PHS also includes an increase of $63 million to address the unacceptably high rate of infant deaths through funding innovative ways to increase access to health care for pregnant women and their infants. Finally, the budget includes $206 million, plus $27 million in advance funding, to address the health problems of our nations homeless population.

RURAL HEALTH

Mr. Roybal: What specific changes have been targeted by the DHHS and the Office of Rural Health to positively affect rural health care access and quality?

Secretary Sullivan: The 1991 budget includes an estimated $371 million to provide access to health care for rural Americans. Of this amount, $327 million will provide health services to rural communities and $44 million will support research which will evaluate the unique circumstances facing providers and consumers of rural health care.

The Office of Rural Health Policy (ORHP), as our principal organizational locus for Departmental leadership and coordination, will continue to evaluate the impact of Medicaid and Medicare policies on rural medical facilities; surveying the access to, and quality of, rural health care services; collecting and disseminating information on rural health care research and innovations; and supporting the activities of the National Advisory Committee on Rural Health. Specific activities planned for 1991 include funding projects which seek innovative solutions for rural communities in danger of losing access to health care, establishing a clearinghouse for rural health care information, and continuing support of seven ongoing research and

outreach programs, as well as continuing a third year grant to the Texas Tech University MEDNET interactive communications network. We have requested $4.4 million for ORHP activities in 1991.

In addition to the activities funded through the Office of Rural Health Policy, other PHS agencies are involved in rural health issues. Our budget proposes: CDC to spend $11 million to research farm safety and health; NIH to spend $19 million on rural cancer, environmental health, aging and nursing research activities and $4 million on National Library of Medicine Outreach; ADAMHA to spend $7 million on rural mental health research and $2.4 on mental health services; AHCPR to spend $2.5 million to study rural health service delivery systems; and HRSA to spend $41 million on National Health Service Corps scholarships and loans to increase the number of health professionals serving rural communities, to spend $257 million on services provided through Community and Migrant Health Centers, to spend $14 million to provide rural infant mortality prevention services, and to spend $9 million on services for the rural homeless.

In 1991, Medicare payments to rural hospitals would also receive a more lenient capital payments reduction of 15% rather than the 25% reduction proposed for urban hospitals; criteria for qualifying as a Sole Community Hospital would continue to be relaxed; and the Rural Health Transition Grants program will continue to strengthen access to necessary care for Medicare beneficiaries.

Mr. Roybal: While a lot of attention has been focused on hospitals, what has been done for ambulatory care, nursing homes, home care, and emergency medical services?

Secretary Sullivan: HCFA has implemented an expansion of the swing bed program to hospitals with 50 to 100 beds, thus increasing the number of skilled nursing beds. In addition the Rural Health Clinics Program provides that Medicare and Medicaid payments can be made to rural health clinics where nurse practitioners and physicians assistants furnish care without the direct supervision of a physician.

The Department also has several demonstration projects in recognition of the demographic and economic changes that have bade it difficult to maintain full service, high quality hospitals. HCFA has provided development funds for a 4-year demonstration in Montana that will provide care at a

level midway between a rural health clinic and a hospital. The Office of Rural Health Policy is also funding a Texas Tech telecommunications program designed to improve quality in rural hospitals by using state-of-the art telecommunications equipment to link university-based teaching physicians and rural physicians. In addition, our new Agency for Health Care Policy and Research will be pursuing an agenda that includes research on rural primary care, including emergency medical services, to examine the impact of the rural economic recession and relationship between health status and access to primary care.

ELDERLY MENTAL HEALTH

Mr. Roybal: Given that most experts feel the elderly are still underserved what federal actions will the Administration take this year to adequately meet the mental health needs of our elderly population?

Secretary Sullivan: The request for the National Institute of Mental Health (NIMH) includes $42 million for aging activities and $27 million for research on Alzheimer's Disease.

Mr. Roybal: What percentage of the Alcohol, Drug Abuse and Mental Health Block Grant was set aside for elderly mental health services?

Secretary Sullivan: The Anti-Drug Abuse Act of 1988 which extended authorization of the ADMS Block Grant did not establish a set aside for elderly mental health services.

MENTAL HEALTH TRAINING

Mr. Roybal: What percentage of the block grant funding was used for professional mental health training programs at the state level?

Secretary Sullivan: Due to the restraints which have existed on collecting information on the expenditure of Block Grant funds we do not have this information. The authority created through the Anti-Drug Abuse Act of 1988, however, now permits us to collect data on State expenditures. Statute permits us to set-aside 5-15 percent of Block Grant funds for this purpose. In future years, we may be better able to answer important questions like the one you asked.

NURSING SHORTAGE

Mr. Roybal: Nursing Shortages: Considering that the nursing shortage problem is still from being solved, has the Department implemented any of the recommendations made by the Secretary's Commission on Nursing or taken any other actions which directly address the shortage problem in rural and central city areas or nursing homes?

Secretary Sullivan: A number of activities are underway in HHS to implement the Nursing Commission's recommendations which were issued December 12, 1988. The Department is in the process of establishing a new one year Commission on the National Nursing Shortage which will monitor and expand on the Nursing Commission's report. The new Commission hopes to focus on recruitment, retention, career development, effective utilization of nursing personnel, and data collection and information systems. Specifically, the following activities are underway:

- A department-wide Nursing Education Legislation Strategy Workgroup has been formed and is developing goals, assumptions, and principles which will be the basis for the Department's legislative strategy.

- A letter, signed September 12, 1989, by the Assistant Secretary of Health, was sent to the governors of each State requesting information of State health personnel shortages and problems including nursing.

- The Bureau of Health Professions has contracted with Project HOPE to identify deficits in the overall database for nursing requirements.

- The Division of Nursing is funding four demonstration nurse-managed primary care clinics in settings such as student dormitories, elderly housing complexes, daily care centers and mobile vans.

- The request for the National Center for Nursing Research is $35.1 million. Included in its portfolio are 7 studies on the impact of patient care information systems on the quality of care and patient outcomes, and 9 projects focusing on issues such as patients' and nurses' priorities during hospitalization and reorganizations of nursing services.

YOUNG AMERICANS ACT

Mr. Roybal: There is proposed legislation entitled the YOUNG AMERICANS ACT patterned after the Older Americans Act which would establish within your Department a permanent Administration for Children, Youth and Families. The Administration would be responsible for (1) developing a national policy on children, youth and family, and (2) coordinating the efforts of federal, State and local programs to address the dire needs of our nation's youths. As I understand it, the bill has been provided to your office for review. Can you share with us what your thoughts are about the Young Americans Act?

Secretary Sullivan: Given the fact that Strengthening the American Family is one of my explicit management objectives, I am generally very supportive of efforts aimed at helping children and families in need. While I applaud the objectives of the Young Americans Act, I cannot comment on the specific details of the bill until a careful and thorough review has been completed within the Administration.

HEALTH PROFESSIONS TRAINING

Mr. Roybal: With the Administration's major cut back in HRSA's health professions training funding, how will the Department ensure that the disadvantaged (for example, racial/ethnic minorities, poor and near poor, rural and central city residents) receive training assistance?

Secretary Sullivan: I am committed to focussing efforts on disadvantaged and minority students and programs which work toward providing health professionals in designated Health Manpower Shortage Areas.

The Administration's request includes $75 million for health professions programs which are targeted toward minority students, including $17 million for two new health professions programs which are part of our Minority Health Initiative.

As you know, the National Health Service Corps (NHSC) places health professionals in areas with shortages. The NHSC recruitment program, comprised of scholarships and loans, provides needy students the opportunity to receive a health professions education while receiving commitments from these students to serve in Health Manpower Shortage Areas. Therefore, our budget includes $42 million for existing members of the National Health Service

Corps and $64 million for the National Health Services Corps Recruitment program. Of the $64 million, $55 million is part of our Minority Health Initiative.

In addition, three major student assistant programs will continue to exist, including the Health Professions Student Loan program, the Nursing Student Loan program, and the Health Education Assistance Loan program.

QUALITY ASSURANCE IN HEALTH CARE

Mr. Roybal: Given that Medicare quality assurance has now been extended beyond the hospital setting, what specific actions are being taken by the Department to implement a full program of health care quality assurance in the following health care settings: nursing homes, home health agencies, ambulatory health care settings and health maintenance organizations? Are assessments of structure, process and outcome measures being included in each of these settings?

Secretary Sullivan: In 1986, the Department began assessing health care quality in nursing homes by focusing more on the outcomes of care than on the structure and process of care. In 1989, we promulgated new nursing home regulations that will be effective on October 1 and that have significantly altered the focus of the regulations themselves to desired outcomes in nursing home residents. We have refined the outcome oriented survey process as well.

We have recently begun surveyor training preparatory to implementing a new outcome oriented survey process for use in surveying home health agencies. This process includes a statutorily mandated functional assessment tool that we developed for use by surveyors to help them determine whether or not individuals are receiving needed home health services and are experiencing desired outcomes of care.

We continue to include structure and process requirements in both our Medicare provider and supplier regulations and survey processes. However, we are progressively shifting both the regulatory and survey processes toward a greater emphasis on defining desired outcomes of care and methods to assess whether or not beneficiaries of Medicare services actually experience the desired outcomes of care intended.

The Peer Review Organization (PRO) Program also

plays a major role in assuring quality of care. Although primarily directed toward inpatient hospital review, PROs also review care in ambulatory settings to ensure that the care is appropriate and meets professionally recognized standards.

HEALTH MAINTENANCE ORGANIZATIONS (HMO) AND OTHER MANAGED CARE

Mr. Roybal: What problems (i.e., marketing, financial solvency, provider payments, beneficiary complaints, selective enrollments/disenrollments) have been encountered in the use of HMOs?

Secretary Sullivan: Enrollment in Medicare risk HMOs has continued to grow slowly but steadily, with an average monthly increase in excess of 13,000 beneficiaries. The majority of contracting plans realize that it is in their best interest to meet or exceed contract requirements to increase member satisfaction among their Medicare enrollees and to generate new enrollment.

During the past year a number of plans with few or no Medicare enrollees dropped out of the program, with the result that the number of contracts has decreased. Many national organizations, however, (Kaiser, FHP, Humana, Pacificare) are committed to the Medicare market and have remained with the program and expanded in some areas. Issues such as the payment methodology and external quality review continue to concern those organizations. Potential new contractors may be awaiting the results of efforts to resolve some of the payment concerns and quality review issues before they enter the Medicare market.

In terms of problems found in the use of HMOs and CMPs, it is our belief that there are no widespread operational problems in the Medicare HMO/CMP program. HCFA has continued its monitoring effort, and reviews performance associated with each of the areas you mention, as well as reviewing quality assurance mechanisms, availability and accessibility of care, and the adequacy of grievance procedures. All Medicare-contracting HMOs/CMPs are reviewed at least every other year. A corrective action plan is implemented when appropriate.

Mr. Roybal: What oversight has been conducted to assure that beneficiaries receive quality health care within HMOs?

Secretary Sullivan: HCFA conducts proactive and comprehensive monitoring activities including the following:

- In October 1989, HCFA began the second two-year cycle of monitoring reviews of Medicare risk and cost contractors. Regional and Central Office staff carry out joint site visits to review the contractor's compliance with regulatory eligibility requirements, as well as contractual requirements.

  By the end of last fiscal year, all HMOs/CMPs which had contracts in effect for at least six months had been under review for compliance with the requirements stated above. Contractors which had deficiencies were required to provide corrective action plans for identified problems. Corrective action is monitored until the contractor is returned to compliance.

- HCFA contracts with Peer Review Organizations (PROs) and Quality Review Organizations (QROs) to review the clinical quality of care provided to Medicare beneficiaries enrolled in HMOs/CMPs with risk contracts. HCFA works closely with the PROs/QROs to obtain coordination of our monitoring activities.

- HCFA recently conducted a survey of 17,000 Medicare beneficiaries who have disenrolled from risk HMOs/CMPs. The purpose of the survey was to understand the reasons for disenrollment, if beneficiaries were encouraged to disenroll to receive needed medical services, or if they disenrolled due to a perceived need for medical services.

  HCFA is currently evaluating the results of the survey and a report of our findings is expected by early summer of this calendar year. The findings from this survey may be used as a basis for continued monitoring of disenrollments from HMOs/CMPs for compliance purposes.

- Approximately two years ago, we implemented a national system for processing complaints received from

beneficiaries enrolled in HMOs and CMPs. Unfortunately, significant inconsistencies in the system have delayed use of the data. By the end of the fiscal year, the data will be tested again for their utility as a program monitoring tool and HCFA will proceed to incorporate the data into its compliance monitoring process.

Mr. Roybal: In the budget, a new managed care initiative, "Medicare Plus", is being proposed. What assurances can you give us that beneficiaries will not be at risk of higher out-of-pocket cost, poorer quality care or inadequate access?

Secretary Sullivan: Our proposal is designed to improve beneficiary access to managed care, lower the cost of comprehensive care, and improve the quality of care. The Medicare Plus program will offer beneficiaries an additional voluntary managed care option. This new proposal will allow beneficiaries to receive health care services through qualified preferred provider organizations. Medicare Plus plans will also provide supplemental Medigap insurance coverage. Plans would have the ability and incentives needed to manage care effectively to help keep premiums affordable. These plans would compete to attract Medicare beneficiaries based on the quality and accessibility of their provider network and on the price and benefit package of their Medigap plan.

PREVENTIVE HEALTH SERVICES AND HEALTH PROMOTION FOR OLDER PERSONS

Mr. Roybal: What demonstration or research projects has the Department conducted or is planning which pilot preventive health services and health promotion for Medicare and Medicaid beneficiaries and assess the effectiveness of including coverage for these services under Medicare and Medicaid?

Secretary Sullivan: HCFA is committed to promoting the concept of preventive health care and has funded various demonstration programs to test the cost-effectiveness of providing certain preventive services not ordinarily covered by the Medicare and Medicaid programs.

Section 9314 of P.L. 99-272 (COBRA 1985) required the Secretary to conduct a 4-year Preventive Health Services Demonstration for Medicare beneficiaries. In April 1988, HCFA awarded cooperative agreements to five Schools of Public Health to implement the Medicare Prevention

Demonstrations. The five schools are Johns Hopkins University, San Diego State University, University of California at Los Angeles, University of Pittsburgh, and University of Washington. A cross-cutting report will synthesize the main findings from the five sites. Report findings will be provided to Congress in the spring of 1991 and 1992.

In September 1985, HCFA awarded a cooperative agreement to the University of North Carolina to develop a Medicare prevention demonstration. This project is similar to the five COBRA prevention demonstrations; findings from this project will be incorporated into the congressional report for the five COBRA projects.

Section 4071 of the Omnibus Budget Reconciliation Act of 1987 mandated a demonstration to test the cost-effectiveness of providing influenza vaccine to Medicare beneficiaries. The demonstration was to begin on October 1, 1988 and last for 24 months. The Report to Congress is due October 1, 1990. If the coverage under Medicare is cost-effective, the demonstration stops, and coverage under Medicare becomes effective November 1, 1990. If the results are inconclusive, the demonstration continues for an additional 24 months until October 31, 1992. The project has been implemented in nine demonstration sites and statewide in four States. We plan to continue the demonstration for the additional 24 months, with the addition of another site plus additional States.

Section 4072(e) of the Omnibus Budget Reconciliation Act of 1987 and Section 6131 of the Omnibus Budget Reconciliation Act of 1989 mandated a demonstration to test the cost-effectiveness of providing therapeutic shoes to Medicare beneficiaries with severe diabetic foot disease. The time frames of the demonstration specified by the legislation are the same as for the Influenza demonstration. The project was implemented in August of 1989 in the States of California, New York, and Florida. The demonstration will need to continue for the additional 24 months specified in the legislation until October 31, 1992.

The National Institutes of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health and the Health Care Financing Administration (HCFA) are currently supporting a congressionally mandated multicenter clinical trial entitled "Modification of Diet in Renal Disease (MDRD)." The primary purpose of this study is to determine the effect of protein and phosphorous restriction, as well as blood pressure

control, on the progression of renal disease. HCFA is paying for the clinical laboratory and nutritional supplements of the trial and has the responsibility for conducting the cost-effectiveness study, if the therapy is found to be effective in delaying renal disease. Other costs of the trial are being paid by NIDDK. The clinical trial is scheduled to end in December 1992 with data analysis to be performed in 1993.

SOCIAL SECURITY ADMINISTRATION

Mr. Roybal: There has been renewed discussion by some in the Administration, including at the Social Security Advisory Commission, about the Privatization of Social Security and/or Medicare. Those of us who have spent our lives defending these important programs are concerned about this. Can you guarantee or provide us with assurances that this Administration will not endorse an effort to move towards changing the fundamental social insurance nature of Social Security and Medicare?

Secretary Sullivan: You can be assured that I remain firmly opposed to any proposal which breaks faith with the 1983 Bi-partisan agreement on Social Security. I am deeply committed to maintaining the integrity of the Social Security System.

As you may know, the President's budget includes a legislative proposal which protects trust fund reserves. The proposal would essentially require that the Treasury annually outlay into a special fund an amount equal to the annual surplus in the Social Security trust funds. That fund would then be used to retire the existing debt.

The proposal will have absolutely no effect on the balances of the Social Security trust funds, so balances will continue to accumulate for benefit payments well into the next century. It will also accomplish the dual task of protecting trust fund balances and retiring a portion of the national debt.

WHITE HOUSE CONFERENCE ON AGING

Mr. Roybal: The last reauthorization of the Older Americans Act (1987) gave the President the authority to call for a White House Conference on Aging in 1991 and authorized $9 million for this purpose. Do you plan to hold a conference in 1991?

Secretary Sullivan: Yes, we plan to hold a White House Conference on Aging in 1991. For the record, the Older Americans Act authorizes such sums

as necessary for FYs 1989, 1990 and 1991.

Mr. Roybal: If yes, is any planning presently going on in preparation for the Conference? What funds are being used for this planning?

Secretary Sullivan: Administration staff are currently developing and reviewing options for a 1991 White House Conference. Federal salaries and expenses appropriations are being used to fund these preliminary planning activities. Formal Conference Planning activities will not take place until the President actually calls for a Conference.

Mr. Roybal: What is your estimate of the total cost for the conference?

Secretary Sullivan: We anticipate that with the $1 million provided we will be able to conduct a focused conference that will contribute significantly to developing an aging policy agenda for the coming decade.

LONG TERM CARE

Mr. Roybal: Is it your opinion that our nation's policy should continue to be one that requires an elderly couple or young parents to be forced into poverty to get some assistance? If not, is it possible to provide such assistance without new revenues?

Secretary Sullivan: In June, I appointed the Quadrennial Advisory Council on Social Security. The Advisory Council is a bi-partisan group representing business, labor, health care providers, politicians and private citizens. Along with issues relating to the uninsured, this group will also study the issue long term care and will submit their report and recommendations later this year.

In addition, Under Secretary Horner is chairing a Department task force that is examining, among other issues, long term care. The task force will look very carefully at different approaches to this problem and will provide a report recommending reasonable and cost effective approaches later this year. Finally, the Pepper Commission is expected to report its recommendations on health insurance for the uninsured in March.

Once we receive the recommendations of these various distinguished groups we can begin to asses the options that are available for addressing this most pressing and very complex issue.

Although we do not have any specific long term care proposals in the budget, currently the Medicaid program provides chronic, long-term care in nursing facilities to persons who are eligible for Medicaid, primarily through SSI or a State's medically needy program. In the past spouses of institutionalized individuals were often left in the community with insufficient resources. Provisions in the Medicare Catastrophic Coverage Act have attempted to prevent this spousal impoverishment. These Medicaid provisions have been retained despite the repeal of the Medicare legislation. Additionally, States also have the option of providing services to persons in home or community based settings through waivers.

MINORITY AIDS ACTIVITIES

Mr. Roybal: The budget requests $1.7 billion for the fight against AIDS. Have we done enough to target black and Hispanic communities to educate them about the scourge of AIDS and about preventative measures? What else should we be doing to deal with AIDS in the black and Hispanic communities?

Secretary Sullivan: It is estimated that in 1991, PHS will spend at least $118 million on AIDS prevention, services, and research activities directly targeted to minorities. This is a $17 million, or +17%, increase above 1990. This includes a request of $48.3 million for special minority AIDS prevention initiatives by CDC, representing a $3.3 million, or +8%, increase. The Office of Minority Health in OASH expects to spend 14% more in 1991 on minority AIDS activities for a total of $4.6 million. Within the NIH budget, $65.5 million, an increase of $13.3 million, or +26%, is proposed for AIDS research efforts focused on minority populations. In addition, PHS estimates that it will spend about $526 million, a $47 million, or +10% increase, on other AIDS research, services, and prevention/ education activities aimed at the general public and at high-risk populations, which should significantly benefit minorities since they are disproportionately affected by AIDS and HIV infection.

Mr. Roybal: Do you agree that in addition to funding State Departments of Health, we need to increase direct funding to community based organizations (CBOs) in order to target more effectively AIDS services to the black and Hispanic communities?

Secretary Sullivan: The 1991 budget request includes support to 32 national and regional

minority organizations, and about 64 minority and other community-based organizations (CBOs) in 27 high-incidence metropolitan areas for AIDS education projects. CDC funds provided through the U.S. Conference of Mayors will also support another 23 minority CBOs on AIDS prevention.

PEDIATRIC AIDS

Mr. Roybal: What are your latest estimates as to the problem of pediatric AIDS in these two communities?

Secretary Sullivan: As of December 31, 1989, a total of 1,995 pediatric AIDS cases have been reported in the U.S. since 1981. Of these, 1,050 cases, or 53%, have been in Black children; and 491 cases, or 25%, have been in Hispanic children.

FEDERAL OFFSET EXPENDITURES

Mr. Roybal: By program, what is your Department's estimate of Federal offset expenditures for FY 1990 and FY 1991?
-The Administration's budget request estimates the Federal offset for FY 1991 to be $160 million while proposing that $301.1 million be made available to States. I understand that your Department interprets the Federal offset as including only Federal costs of Medicare provided to aliens legalized under Section 254 of IRCA.

Secretary Sullivan: The Federal offset, Federal cost for primarily Medicaid and some Food Stamps, is estimated at $160 million for FY 1991. The $301.1 million that would be obligated to the States in FY 1991, combined with unused funds from prior years, would enable States to double FY 1989 outlay rates in FY 1990, 1991, and 1992. The Inspector General has made recommendations similar to the one proposed.

Mr. Roybal: If the Federal offset is estimated to be $160 million in FY 1991, should not State and local expenditures for all of public health, public assistance, and educational services which are potentially reimbursable by SLIAG funds far exceed $301 million?

Secretary Sullivan: States will have $1.3 billion in prior year funds as well. The Federal offset estimates for all four years, 1988-1991, total $420 million, $528 million less than original estimates made two years ago. Lower State Medicaid

costs free up another $500 million. Thus, States can expect to have $1 billion more for other purposes.

SLIAG

Mr. Roybal: What is your Department's estimate of total State and local legalized alien costs in FY 1991 which are potentially reimbursable by SLIAG costs?

Secretary Sullivan: Under our proposal, States would have $1 billion remaining after FY 1991.

Mr. Roybal: For FY 1990 and FY 1991, what is your Department's estimate of the total State and local share of legalized alien Medicaid costs, including for special agricultural workers whose costs are not subject to the Federal offset?

Secretary Sullivan: We estimate $160 million for the Federal share of Medicaid costs. We do not have separate estimates for Special Agricultural Workers. The overall State and local shares are estimated at $126 million.

Mr. Roybal: The Administration is proposing to amend IRCA as follows: "Funds appropriated for fiscal years after 1990 for grants to States under section 204 (b) of Immigration Reform and Control Act of 1986 shall not exceed a total of $301,027,000, which shall be available for obligation in fiscal year 1991 only, notwithstanding section 204 (a) of said Act, as amended. Is it your Department's interpretation that the above language would affect the current ability of States to carry over unobligated funds from one year to the next? For example, would it mean that no SLIAG funds can be carried over beyond FY 1991?

Secretary Sullivan: We expect States would carry forward $1 billion into 1992 under our proposal. The Department does not eliminate the carry forward authority of unused FY 1991 funds in our proposed appropriation language.

REFUGEE ASSISTANCE

Mr. Roybal: What are your Department's budget assumptions regarding the cash assistance dependency rates of refugees for FY 1990 to FY 1991?

Secretary Sullivan: The estimated eligible population's dependency rate for FY 1990 is 49.4%, and for FY 1991 is 43.5%.

Mr. Roybal: Your Department has a policy of reducing the time period of refugee reimbursement in fiscal years in which the funds appropriated for refugee cash and medical assistance are believed to be insufficient to fully reimburse State and local costs for 36 months as authorized under the Refugee Act of 1980. I understand that, for FY 1990, effective January 1, 1990, your Department is limiting reimbursement of State and local costs for AFDC, Medicaid, and SSI provided to refugees in the U.S. for only four months or less.

In the event that the funds appropriated for refugee cash and medical assistance in FY 1990 exceed the amount needed to fully reimburse States under the 4-month reimbursement policy, how would your Department allocate the surplus among the States?

Secretary Sullivan: In consultation with the States, the Department adjusted subsidies to fit the appropriation. The Department has not limited the period of Federal reimbursement to the States to four months or less. We have estimated the number of months it is likely that the $210 million that Congress appropriated for cash and medical assistance will provide reimbursement. It is possible that the $210 million will provide more than four months of reimbursement to the States.

Mr. Roybal: What is your Department's estimate of the amount of funding that would be needed in FY 1991 to fully reimburse State and local costs of cash and medical assistance (including administration) provided to refugees in the U.S. for 36 months or less, as authorized under the Refugee Act of 1980? In developing the estimate, assume that special cash and medical assistance provided to needy refugees who are categorically ineligible for AFDC and Medicaid would be limited to 12 months.

Secretary Sullivan: Federal reimbursement to the States for a 36/12 month period of refugee cash and medical assistance, including administration, would cost an estimated $400 million in FY 1991, or a $190 million increase over the current request.

MINORITY HEALTH

Mr. Stokes: I do have two questions about the OMH request. You propose that $11 million of the increase be used for coordination of National public and private minority health efforts. Could you give us specific examples of the kind of efforts that might be supported?

Secretary Sullivan: The $11 million increase will fund Minority Community Health Coalition Grants; PHS interagency agreements, such as NIH research; assistance to states and private sector groups; re-examination of the Secretary's 1985 Task Force Report findings; workshops and administrative/ management support; and targeted minority AIDS activities.

Mr. Stokes: Why is only $1 million of the increase targeted toward minority HIV/AIDS initiatives?

Secretary Sullivan: OMH is not the only area in which minority directed AIDS activities are supported. Throughout the PHS, we are requesting over $118 million on AIDS programs which directly affect minorities as well as $527 million indirectly targeted to minorities. In OMH, we are specifically seeking $4.6 million in 1991.

HEALTH CARE SYSTEM QUALITY REVIEWS

Mr. Stokes: In his State of the Union Address, the President stated that you will lead a domestic policy council review of recommendations on the quality, accessibility and cost of our nation's health care system. As you know, I serve on the Pepper Commission, which has a similar mission. Can you tell us a little bit more about how you plan to meet your charge? How will this review differ from the work undertaken by the Quadrennial Commission on Social Security chaired by Deborah Steelman?

Secretary Sullivan: The intent of the Domestic Policy Council is to review the recommendations of the various groups that are currently meeting to study our nation's health care system.

In June, I appointed the Quadrennial Advisory Council on Social Security. The Advisory Council is a bi-partisan group representing business, labor, health care providers, politicians and private citizens which is studying our health care system

with emphasis on the uninsured. They will submit their report and recommendations later this year, with interim recommendations relating to the uninsured as soon as possible.

In addition, Under Secretary Horner is chairing a Department task force that is also examining problems in the health care system, including the uninsured and long term care. The task force will look very carefully at different approaches to this problem, including extending Medicaid to the uninsured, and will provide a report recommending reasonable and cost effective approaches later this year. Finally, the Pepper Commission is expected to report its recommendations in March.

Once we receive the recommendations of these various distinguished groups, the Policy Council can begin to assess the options that are available for addressing this most pressing and very complex issue.

Mr. Stokes: Are funds requested in the President's budget to support this review?

Secretary Sullivan: We do not have any funds specifically allocated in the FY 1991 HHS budget for this activity since it can be accomodated within our budget for administration.

PEDIATRIC AIDS

Mr. Stokes: Although the number of pediatric AIDS cases is increasing at an alarming rate, I understand that you are requesting only $14.7 million for pediatric AIDS demonstration grants, a decrease of $68,000 from the FY 1990 level. What percentage of the AIDS budget is targeted toward pediatric AIDS?

Secretary Sullivan: HHS will spend about $172 million in total in 1991 directly on pediatric AIDS. This is an increase of $35 million, or +26%, over 1990 and $74 million, or +75%, over 1989. While the 1,995 pediatric AIDS cases reported to CDC as of December 31, 1989, are less than 2% of the total number of AIDS cases, the $172 million request for directly targeted pediatric AIDS resources represents about 10% of the total PHS and OHDS AIDS budgets for 1991.

The pediatric AIDS demonstration grants in HRSA, one part of the total Departmental pediatric AIDS effort, are proposed to be funded at $14.8 million in 1991, the same level as was appropriated in 1990.

HUMAN GENOME PROJECT

Mr. Stokes: Mr Secretary your statement indicates that you are requesting a $48 million increase for human genome research supported by the National Institutes of Health. For 1990, Congress made over $60 million available for NIH's Human Genome project. Given other pressing needs in the area of health care, why should we invest this amount of money into the Genome project?

Secretary Sullivan: The Human Genome Initiative is a world-wide research effort focusing on analyzing the structure of human DNA. With the information gained from the research we hope to support, scientists will be able to better understand, diagnose, prevent, and treat, many of the more than 4,000 genetic disorders (such as Huntington's Disease and Sickle Cell Anemia) which afflict mankind. Furthermore, new technologies discovered during the course of the initiative will also have applications in agriculture and environmental science.

During 1991, the initiative will focus on technology development and on training a full complement of multifaceted scientists (physicists, mathematicians, computer scientists, molecular biologists). Special efforts also will be made to enhance close working relationships with the private sector to facilitate the transfer of technology and information to industry and the medical community.

In a survey conducted by the Industrial Research Institute of its 257 member companies, the Human Genome Project was the most popular Federally funded research and development program. The genome project ranked higher than the Space Station, Strategic Defense Initiative or the Superconducting Super Collider.

DRUG TREATMENT

Mr. Stokes: Use of Crack Cocaine and other illegal drugs has reached epidemic proportions in this country. You have included $1.7 billion for drug treatment and prevention programs in your Department. Do you believe that this amount is enough to ensure treatment on demand for drugs abuse? What will it take to accomplish this?

Secretary Sullivan: I am committed to providing quality treatment to those persons suffering from a drug addiction. However, we believe the term "treatment on demand" is a

misnomer. Treatment on demand often results in "revolving door" treatment where addicts do not go to treatment to end addiction. Instead, we believe accountability and matching the right treatment to the type of addiction and the addict's needs is essential to providing quality treatment.

The Federal government is only one source of drug treatment funding. State and local governments, third party insurers, and private funding sources are all important elements in providing treatment. While our budget increases the availability of treatment (Federally funded treatment slots increase by 4,000 and each treatment slot treats approximately 2.5 people a year), the Federal government has the responsibility to improve the quality of treatment provided. The Office for Treatment Improvement will be working with States and other treatment providers in improving the quality of treatment. Also, the research conducted by the National Institute on Drug Abuse on research modalities and medications development are crucial steps in treating drug abuse.

Mr. Stokes: In a statement following the release of the President's Budget, the U.S. Conference of Mayors criticized not only the amount of money for drug treatment proposed by the President, but also the mechanism by which it is provided. The mayors stated that by providing these funds as block grants to the States, the areas that are most impacted by the drug epidemic--cities--are not receiving enough funds to enable them to combat the problem. Do you believe that we need a different funding mechanism to ensure that sufficient funds go directly to the cities?

Secretary Sullivan: Currently, the Department has a number of funding mechanisms for drug treatment. The largest of these mechanisms, the ADMS Block Grant ($577 million for drug abuse activities in FY 1991), does not preclude cities from receiving treatment funds. Instead, the block grant mechanism allows each governor and State legislature to determine the needs and resources within their State and allot Federal resources and State resources accordingly.

Other Federal programs such as the Drug Treatment Grants for Crisis Areas and Treatment Improvement Grants provide funds for drug treatment through evaluating grant applications, which may be submitted by cities. One of the areas which the new Office for Treatment Improvement (OTI), headed by Dr. Beny Primm, will focus on is cities. Also, the Office of Substance Abuse Prevention (OSAP)

places emphasis on populations which are predominant in cities such as high risk youths and pregnant women.

National Drug Control Strategy II has designated five areas as High Intensity Drug Trafficking Areas. The Strategy concentrates $1.4 billion for drug enforcement, treatment, and prevention activities in these five areas. Four of the five areas are major cities -- Houston, Los Angeles, Miami, and New York.

DISCRETIONARY REQUEST

Mr. Early: Mr. Secretary, in your statement, you indicate that the appropriations request before this Committee is $136.8 billion, an increase of almost 10 percent over the FY 1990 level. What is the Department's request for domestic discretionary programs and what is the dollar and percentage increase over the FY 1990 level for these programs?

Secretary Sullivan: The discretionary budget authority requested is $21.8 billion, $529 million or 2.4 percent over FY 1990. For programs under the jurisdiction of this Subcommittee, the discretionary budget authority request is $20.1 billion, $539 million or 2.7 percent over FY 1990.

We feel a more accurate measure of discretionary resources is the program level, which includes trust fund limitations, user fees, and advance funding already appropriated in addition to the budget authority. This request is $27.4 billion, $1.4 billion or 5.4 percent over FY 1990. For programs under the jurisdiction of this Subcommittee, this request is $25.4 billion, $1.2 billion or 5.3 percent over FY 1990.

Mr. Early: What is the total increase proposed for discretionary programs.

Secretary Sullivan: Total increases for discretionary programs are $2.3 billion. A table reflecting **major** increases and the amount of increase follows:

Program	Increase
OHDS	$510 million
NIH	$414 million
LAE	$330 million
ADAMHA	$306 million
HRSA	$281 million
HFCA - Prog. Mgmt.	$194 million
IHS	$100 million
FDA	$91 million

Mr. Early: What is the total decrease proposed for discretionary programs?

Secretary Sullivan: Decreases for discretionary programs total $1.2 billion. A summary of **major** decreases follows:

SUMMARY OF DISCRETIONARY PROGRAM DECREASES

Program	Decrease
OCS	$366 million
LIHEAP	$343 million
HRSA	$188 million

LIHEAP

Mr. Early: The President's budget proposes a $343 million, or 24.6% decrease in the low-income energy assistance program. Funds for this program have been steadily decreasing. Why is such a large reduction being proposed in this program?

Secretary Sullivan: We believe it is time to reassess the Federal government's financial role in providing energy assistance benefits to the States. The inflation-adjusted price of fuel will continue its long-term decline in FY 1991, reaching the levels that existed before the price increases of the late 70s which led to LIHEAP becoming a major program.

Mr. Early: What impact will this proposal have on the number of people being served?

Secretary Sullivan: Because LIHEAP is a block grant which affords the grantees flexibility in designing their energy assistance programs, there is no direct correlation between reductions in Federal appropriations and households served. Thus, we are unable to estimate the number of households served at any level of Federal appropriations. LIHEAP grantees may supplement their Federal appropriation with State or oil overcharge monies, not exercise their option to transfer funds out of LIHEAP into other block grants, eliminate a services component such as cooling or weatherization or reduce the size of the benefit provided. LIHEAP grantees could have increased FY 1990 funding by 20 percent by transferring funds from other block grants.

Mr. Early: As you know, the New England States, along with many others, have experienced an exceptionally cold late November and December accompanied by sky-rocketing retail increases in fuel; the price of home heating oil jumped more than 50%. A number of programs have exhausted or almost exhausted their fuel assistance funds. What is the department's position with respect to a supplemental for this program?

Secretary Sullivan: The budget as submitted does not include a supplemental appropriation for

LIHEAP. The problematic situation that occurred due to unexpected severe weather conditions in December and high oil prices was an aberration, which apparently impacted the population served by LIHEAP to different degrees; the most significant areas affected are being those which use bulk fuel oil and where weather conditions were the coldest. Although December was 27% colder than normal, January was 24% warmer than usual. The National Weather Service predicts an average winter season, October through April. Further, wholesale oil prices have dropped to pre-December levels and retail prices have continued to decline as well.

Mr. Early: What steps, if any, is the Department taking to address the problem of States or programs which have exhausted or nearly exhausted their fuel assistance funds?

Secretary Sullivan: Some States have received third quarter grants early. We are reviewing requests from Governors on a case-by-case basis.

Mr. Early: One of the arguments make in defending proposed reductions in the Low-Income Energy Assistance Program is that a number of States transfer funds out of this program. What is the Department's position on eliminating this transfer out authority?

Secretary Sullivan: States also have the authority to transfer funds into LIHEAP. The flexibility given to the States by the transfer rules enables them to focus funds on what they perceive as their citizens' greatest needs.

MATERNAL AND CHILD HEALTH

Mr. Early: Your budget request includes $25 million for a new "one-stop-shopping" program in the area of maternal and child health. Why is this initiative important? Would you summarize how this program would work?

Secretary Sullivan: The new "one-stop shopping" program will be administered in conjunction with the Maternal and Child Health Block Grant. This grant program is designed to encourage States to coalesce and coordinate health and welfare services available to pregnant mothers and infants, simplifying service accessibility to the clients.

Mr. Early: Your request also includes $36 million for case managed care for pregnant women. How would this program work and what is the relationship of this proposal to the "one-stop-

shopping" program? Where in your budget are these funds being requested?

Secretary Sullivan: I am committed to reducing the rate of infant mortality in this country. Within PHS, our budget includes $63 million for our Access Initiative which specifically addresses reducing infant mortality. The two programs in question, the "one-stop shopping" program and the infant mortality initiative (case managed care), are part of this initiative. Both of these programs are part of the Health Resources and Services Administration's budget.

The programs address two different problems. The infant mortality initiative provides case managed care for individual mothers and infants in need of health care services and counseling throughout pregnancy and the first year of the baby's life. The "one-stop shopping" program encourages States to establish or improve the system that provides health and social services to these women and children.

HEALTH PROFESSIONALS

Mr. Early: Why are you proposing to eliminate funds for health manpower programs in such as primary care and public health, when studies have indicated a continuing, if not increasing for personnel in these areas?

If I recall correctly, a recently released Institute of Medicine study calls for increasing the number of primary care residents. Do you plan to reconsider your request for eliminating funds for these programs?

Secretary Sullivan: I am committed to focussing a good portion of our efforts on disadvantaged and minority students and programs which work toward providing health professionals in designated Health Manpower Shortage Areas.

The Administration's request includes $75 million for health professions programs which are targeted toward minority students, including $17 million for two new health professions programs which are part of our Minority Health Initiative.

As you know, the National Health Service Corps (NHSC) places health professionals in areas with shortages. The NHSC recruitment program, comprised of scholarships and loans, provides needy students the opportunity to receive a health professions education while receiving commitments from these

students to serve in Health Manpower Shortage Areas. Therefore, our budget includes $42 million for operational expenses for existing members of the National Health Service Corps and $64 million for the National Health Services Corps Recruitment program. Of the $64 million, $55 million is part of our Minority Health Initiative.

In addition, three major student assistant programs will continue to exist, including the Health Professions Student Loan program, the Nursing Student Loan program, and the Health Education Assistance Loan program.

Mr. Early: The budget also proposes to eliminate funds for nurse training programs. Has the nursing shortage ended? Are we projecting that we will need fewer nurses in the future?

Secretary Sullivan: Our FY 1991 request does include $4 million for nurse training through our health professions program as well as $13 million available through the nursing student loan revolving fund.

Some of the latest information available suggests that there might be a slight easing of the nursing shortage, at least in some areas. The vacancy rate for registered nurses in hospitals has declined slightly between December of 1987 and 1988, from 11.3 percent to 10.6 percent, according to the latest data available from the American Hospital Association. First-time enrollments in basic nursing education programs have shown some increases, rising 4.3 percent to 94,594 in the 1987-1988 academic year over the total of 90,693 in 1986-1987; and indications are that first-time enrollment levels may show some increases in 1988-1989 as well.

The Commission on Nursing assessed the cause of the nursing shortage as stemming from the increases in employer demand. The March 1988 National Sample Survey of Registered Nurses reinforced such a conclusion. The survey showed that more nurses were employed than ever before -- 1.6 million compared to 1.5 million found in the November 1984 sample survey. It also showed that a higher proportion (eighty percent) of all licensed registered nurses are employed in nursing than previously.

HEALTH PROMOTION AND PREVENTION PROGRAMS

Mr. Early: Mr. Secretary, there has been a great deal of discussion and emphasis on the need for health promotion and prevention programs. And, we know that there are a number of areas where

effective steps can be taken. Although you are proposing an $80.9 million increase for CDC, a little more than 80% of the increase is for AIDS activities, with most of the remainder for epidemiological activities related to infant mortality. Programs such as the STD program, immunization, chronic disease prevention, and lead poisoning are basically level funded. Why didn't the Department propose increased funds for these activities?

Secretary Sullivan: The 1991 budget request for CDC of $1,172 million represents an overall increase of 7%, or +$87 million over 1990. This includes a 15% increase for AIDS and a 2% increase for non-AIDS activities. Even though more people are currently affected by other infectious and chronic diseases, we believe our extraordinary efforts to fight AIDS and HIV infection are still warranted and command a higher priority at this time. This is the case for several reasons. AIDS is an infectious disease, which, if not kept in check now, could grow into an even larger epidemic. AIDS can lie hidden for years, without symptoms, in those who are infected, and the virus can be transmitted during this time. Most importantly, AIDS is still virtually fatal; available AIDS drugs, such as AZT and aerosolized pentamidine, only delay the progression of the disease, not cure it. AIDS, unlike many other causes of death, primarily strikes young Americans in their prime. AIDS is also now the ninth leading cause of death among children 1 to 4 years of age, and the seventh in young people between the ages of 15 and 24. Racial and ethnic minority populations are increasingly disproportionately affected by the epidemic, including about 43% of all reported cases to date. We also believe that finding the keys to unlock the AIDS mystery will help many others with other diseases. We are already beginning to see spin-offs from our AIDS work into other areas such as immunology, cancer retroviruses, and minority health education.

Furthermore, while the request for CDC's Sexually Transmitted Disease (STD) budget did not receive a further increase in 1991, the successful implementation of information and education programs to prevent the spread of AIDS/HIV by changing sexual and other high-risk behaviors, for which CDC's 1991 budget has been increased by about $66 million, should have a positive effect on reducing all STDs. More directly, CDC is currently working to ensure that all State and local AIDS prevention activities also support syphilis control efforts. In addition, it appears that the rise in crack-cocaine usage and

the practice of exchanging sex for crack is also a cause for rising STD cases. Our major push to expand anti-drug abuse prevention and treatment efforts should therefore also contribute to controlling STDs. Throughout the PHS, funds for these anti-drug abuse activities are proposed to be increased in 1991 by $162 million, or +13% over 1990, and by $629 million, or +85% over 1989 levels.

The 1991 budget request also maintains the 17% increase Congress added in 1990 to CDC's Chronic and Environmental Diseases activities, including significant expansions in areas such as breast and cervical cancer screening, lead poisoning prevention, injury control, and disabilities prevention. A total of $79 million is requested for these programs in 1991. In addition to these CDC monies, the National Institutes of Health (NIH) also spends billions of dollars annually on basic and clinical research related to chronic health problems, such as cancer, cardiovascular diseases, and chronic lung diseases. The 8.5% increase provided to the CDC immunization program in 1990 to support new efforts in preventing the perinatal transmission of hepatitis B and conducting outreach efforts to encourage parents to follow the appropriate immunization schedule for their children is also maintained within the 1991 request of $152.7 million for all immunization activities. Furthermore, the 1991 budget continues to support the $3.9 million Congress added in 1990 for categorical grants for childhood lead poisoning prevention programs with the States.

Mr. Early: What impact will the CDC budget request for programs such as these have on the Department's ability to meet health goals of the Year 2000? Will we lose ground before we start?

Secretary Sullivan: We believe the 1991 budget request for CDC of nearly $1.2 billion allows CDC to continue to provide aggressive leadership for moving the Nation in the direction of meeting the health challenges of the 1990's and toward achieving the national health objectives for the Year 2000. Emphasizing prevention remains one of the Department's top priorities because it helps to control health care costs, reduces human suffering, and improves our Nation's health care status. Preventing disease and disability is not only cost-effective, but it also keeps our citizens more productive. On top of CDC's funds, we estimate that the 1991 budget request includes more than $4.8 billion, an 8.4% increase over 1990, for other prevention-related research, disease control, health

promotion, and nutrition services throughout other agencies of the Department.

It must be noted that meeting the national health objectives for the Year 2000 cannot be accomplished if they are viewed as the sole responsibility of the Federal government. Achieving success will require the strong commitment of our partners in State and local health departments; private sector health care practices; medical, nursing, and public health schools, and voluntary advocate organizations. Even more important to progress is the need for the individual to take personal responsibility for his or her health by recognizing that lifestyle choices related to smoking, diet, exercise, alcohol, and other drugs are the most important factors in helping them live longer and healthier lives.

BREAST AND CERVICAL CANCER PREVENTION

Mr. Early: As you know, the FY 1990 bill included funds for a new breast and cervical cancer prevention initiative. Does the FY 1991 request include an increase for this initiative and, if not, why not?

Secretary Sullivan: In total, the 1991 budget will fund about $45.7 million on cervical and breast cancer screening, an increase of $30.1 million over 1990. This includes $40 million, an increase of $30 million over 1990, that HCFA estimates Medicare will spend in 1991 to reimburse for cervical cancer pap smears, implementing the new requirement included in the Omnibus Budget Reconciliation Act of 1989.

In addition, the 1991 budget for CDC maintains the 1990 level of $4.9 million for discretionary grants to States for breast and cervical cancer prevention programs. This continues the expanded program level resulting from the 1990 Congressional appropriation. These funds will be used to initiate in about five States mammography and pap smears screening programs, education programs for women and health care professionals, laboratory and x-ray quality assurance measures, and augmented surveillance systems. The National Cancer Institute (NCI) is also expected to spend $0.8 million in 1991 for a breast cancer screening education initiative.

We would also note that at least 20 States already mandate that private and public health insurers include coverage for breast cancer screening through mammograms. This includes the States of Maryland, Texas, California,

Massachusetts, Arizona, Connecticut, Kansas, Florida, Minnesota, New Hampshire, Oklahoma, New York, Rhode Island, Colorado, Iowa, North Dakota, Tennessee, Virginia, and Washington. Furthermore, at least four States, Kansas, Delaware, Rhode Island, and Minnesota, also now mandate public and private insurance coverage for pap smears. In Ohio, Hawaii, and Maryland, hospitals are required to offer cervical cancer exams to all women within the age of risk of cancer. New York and Maryland have also developed regulations designed to improve clinical laboratory performance on pap smears.

The Medicare Catastrophic Health Insurance legislation that Congress repealed last year contained language that would have provided for mammography screening every 2 years for women 65 years of age and older, or greater frequency for high-risk women. Reimbursement of up to $50 per screening would have been provided.

Mr. Early: Mr. Secretary, in your view, how important is this initiative and where would you rank it in terms of your priorities?

Secretary Sullivan: It is very important that women take advantage of available breast and cervical cancer screening services, regardless of whether they are financed publicly or privately. For example, we could reduce the number of deaths by at least 30% if women who are not getting mammograms would get them.

NIH DIRECTORSHIP

Mr. Early: Mr. Secretary, I'm very concerned that we do not yet have a new director for the NIH. It seems to me that in the past there was no shortage of exceptional candidates. This post has now been vacant for 6 months. When can we expect a new director to be named, and what has been the problem?

Secretary Sullivan: We hope to have a new director named within the next few months. As you may know I have convened a panel of fourteen distinguished biomedical researchers, physicians and research administrators to provide advice to me on how to strengthen the position of the director so that NIH can continue to function effectively as the leader in biomedical research. This advisory panel will help us to better define the role of the NIH director, an effort I believe will make the job more attractive to a highly qualified candidate.

NIH RECRUITMENT AND RETENTION

Mr. Early: In general how would you characterize the current recruitment and retention situation at NIH? To what extent will the recently enacted legislation providing salary increases for senior executives ameliorate the recruitment and retention problems faced by NIH? What additional steps do you feel need to be taken to improve the situation?

Secretary Sullivan: Over the past few years a number of statements have been made with respect to NIH's ability to recruit top scientists. While NIH salaries are not nearly as attractive as those offered to top researchers at many of NIH's extramural grantee institutions, there is no doubt that NIH is still the preeminent biomedical research center in the Nation, if not the world. I would point out that we have been able to recruit several top scientific minds to NIH in the past few years. Dr. James Watson was recruited to head up the Human Genome Initiative, Dr. Ada Sue Hinshaw was recruited to direct the National Center for Nursing Research, and Dr. James Snow recently joined NIH as the new Director of the National Institute on Deafness and Other Communication Disorders. I would also mention that prominent scientists such as Dr. Anthony Fauci, the Director of the National Institute of Allergy and Infectious Diseases, and Dr. Samuel Broder, Director of the National Cancer Institute have chosen to remain on the NIH campus.

With respect to pay, it is not yet clear whether the enacted increase for senior executives will have a significant impact on recruitment and retention. However, the President's Budget does address this issue of pay for top researchers by calling for the establishment of ten endowed chairs for eminent senior biomedical scientists. Recipients of these visiting researcher awards would receive a salary of up to 150 percent of Executive Level II.

Mr. Early: A number of researchers in my state have expressed to me serious concerns about various aspects of the proposed financial disclosure and conflict-of-interest regulations. What is the current status of this effort?

Secretary Sullivan: On September 15, 1989, NIH proposed new guidelines to address potential conflicts-of-interest among extramural research projects supported by NIH. These guidelines were published in the "NIH Guide for Grants and Contracts". In general, the guidelines would

prohibit NIH grantees, or their families, from having a financial interest in the results or potential products of their research.

On December 29, 1989, in light of widespread concern about the effects of the guidelines, I instructed the NIH to rescind the proposed guidelines. Instead, I requested that NIH prepare a set of options for addressing potential conflicts-of-interest which would ensure the integrity of NIH supported research without excessive or counterproductive regulatory impediments. When this process is complete we will issue a Notice of Proposed Rulemaking (NPRM), and allow for a period of public comment on any proposed changes in grantee eligibility or responsibility. At this time we have set no precise schedule for publication of the conflict-of-interest rule.

THE NIH BUDGET

Mr. Early: The budget request before us proposes a 4.7 percent increases overall for the NIH, correct? Mr. Secretary, how would you say the NIH fared in the Administration's budget process vis-a-vis the overall R&D increase? The increase received by other agencies for R&D?

Secretary Sullivan: I understand that the President's FY 1991 Budget calls for an overall increase of 4.5 percent for all federally supported research and development. Thus, I would say that, overall, a 4.7 percent increase for the National Institutes of Health is a fair level of growth over 1990. However, let me also point out that within the total increase, support for NIH basic research in increases by 5.7 percent. Those research mechanisms which primarily support basic research were provided increases which exceed the inflation rate: +5.4 percent for research project grants; +5.5 percent for research centers; and +6.9 percent for intramural research.

Mr. Early: The budget request highlights three specific areas of increases: the human genome project, AIDS, and intramural buildings and facilities. What is the increase proposed for each of these areas in percentage terms compared to FY 90? What is the aggregate increase proposed for these three areas?

Secretary Sullivan: The budget for the National Center for Human Genome Research increases by 81 percent, NIH support for AIDS increases by 7.6 percent, and our request for NIH buildings and facilities is an increase of 45 percent over 1990.

The aggregate increases for these three are, $48.5 million, $56.7 million, and $27.6 million respectively from 1990 to 1991.

RESEARCH BUDGET INCREASES

Mr. Early: What is the overall increase (percent) in the budget request for other research programs (such as cancer, heart, diabetes, etc.)? How do these compare to the inflation factor assumed in the budget, and with the biomedical R&D index which I understand is generally higher than the GNP deflator?

Secretary Sullivan: For 1991, the biomedical research and development price index (BRDPI) is 5.8 percent and the GNP inflation rate is 4.2 percent. The biomedical research price index applies to most of NIH's extramural portfolio and its intramural programs, but obviously, not to accounts such as Research Management and Support, the Office of the Director, or Buildings and Facilities.

The following table shows the percent increase for NIH by institute:

RESEARCH PROGRAM INCREASES BY INSTITUTE

NCI	+3.7%	NIAMS	+4.2%
NHBLI	+3.7%	NIDCD	+4.5%
NIDR	+3.5%	DRR	-5.3%
NIDDK	+4.1%	NCNR	+4.8%
NINDS	+4.4%	NCHGR	+81.5%
NIAID	+6.5%	FIC	+4.5%
NIGMS	+4.7%	NLM	+4.9%
NICHD	+4.2%	OD	-7.7%
NEI	+4.6%	B&F	+45.1%
NIEHS	+2.9%		
NIA	+4.0%		

Mr. Early: The budget request indicates that there is a $227 million increase for research project grants. How much of this increase relates to the proposed increase in funding for the Human Genome project? For AIDS?

Secretary Sullivan: Funds for research project grants supported by the National Center for Human Genome Research increase by $12.3 million dollars, from $40.3 million in 1990 to 52.6 million in 1991. Of the increase in funds for these grants, $26 million will support additional AIDS related grants, increasing this support for AIDS from $290 million in 1990 to $316 million in 1991.

PAYLINES AND AWARD RATES

Mr. Early: Under the FY 91 budget request for NIH, do the payline percentiles and award rates increase or decrease? Is the continuing decline in payline percentiles and award rates of concern to you, Mr. Secretary?

Secretary Sullivan: Overall, NIH projects that the pay line percentiles for 1991 will be somewhat higher than those we expect to experience in 1990. Similarly, the overall award rate projected by NIH for 1991 is higher than that projected for 1990, rising from 24.1 percent in 1990 to 25.4 percent in 1991.

The paylines and award rates are statistics which we continue to watch with great concern. Having said that, I will also point out that the recent decline in paylines and award rates are to some extent the result of decisions to increase the average length of research project grants and to fund large numbers of new and competing grants in recent years. As the non-competing continuation awards consumed an increasingly greater share of the total budget for RPGs, funds for competing awards could not support an increasing number of awards.

Mr. Early: When we discussed declining paylines and award rates last year, you indicated that the great competition for grants may be discouraging new investigators from entering the field. You also indicated that you were greatly troubled by this because these were the individuals we would be looking to 10 to 15 years from now to be the seasoned investigators and leaders in the research community. Is this still a concern? What specifically does the budget request for NIH do to address this concern?

Secretary Sullivan: Encouraging young scientists to come in to and remain in the field of biomedical research is a concern of the NIH and this Department. I understand that the Acting Director of NIH soon will be receiving a set of recommendations which address this and other issues related to the needs for research training and research manpower. We will look at these recommendations to see what approaches will best suit the needs of NIH and the research community.

Mr. Early: Are we seeing more conservative research proposals -- less boldness and innovation

-- because of the intense competition for funding? Are fewer bold and innovative proposals being funded.

Secretary Sullivan: The NIH peer review system for review and approval of grants allows for a wide range of judgements on the degree to which federal support for biomedical research should focus on traditional approaches to research or branch out to more innovative studies. It would be presumptuous of me to try to discern an overall trend in research approaches and then relate it to the dynamics of grant funding. I do believe that there is still a significant level of support for innovative and bold research. As examples, I would point to effort supported as part of the Human Genome Initiative and the search for an AIDS vaccine, areas in which scientists are continuously breaking new ground.

Mr. Early: I'm now hearing that seasoned investigators with top notch proposals (scores in the 150-160, even 140-150 range) are not being funded or are increasingly becoming borderline cases in terms of funding. This is very disturbing; if seasoned investigators begin thinking about leaving the field, we are facing an extremely serious situation. Is this an issue your are concerned about Mr. Secretary?

Secretary Sullivan: Yes, I am concerned about the impact of decreasing paylines discouraging researchers from remaining in the field. In 1991, paylines, as well as the award rates, will increase over the levels expected in 1990.

BUDGET EFFECT ON BIOMEDICAL RESEARCH

Mr. Early: With the exception of the Human genome project and AIDS, how does the President's Budget request "enhance" biomedical research, given declining award rates and priority scores and a further squeeze on the size of grants to stretch the number of new and competing grants over the 5,000 mark?

Secretary Sullivan: The President's Budget provides for an increase of 462 new and competing awards in 1991. This increase in new grants will allow paylines and award rates to increase somewhat over the 1990 expected levels. This reverses the trend of the past four years.

As a general comment I would say that biomedical research is a fluid enterprise; each year brings new discoveries and improved technology. As a consequence, biomedical research is enhanced every

year the federal government supports this nation's health related research efforts. Biomedical research is particularly enhanced by investments in basic research, from which the nation will reap rewards far into the future. The President's FY 1991 Budget therefore, enhances biomedical research by favoring basic research efforts with a 5.7 percent increase.

COMMUNITY SERVICE BLOCK GRANT PROGRAM

Mr. Early: Why are you proposing to eliminate the Community Services Block Grant Program?

Secretary Sullivan: Since this discretionary program was initiated in 1981, there have been institutionalized basic reforms as well as increased funding for such activities as employment services (JOBS), and child development (HEAD Start). We believe community action agencies can and should, provide services on a reimbursable basis like other private non-profit organizations. Given these increases in conjunction with services provided in other Federally funded program areas, the FY 1991 budget includes only $42 million to fund the highly targeted Emergency Community Services for the Homeless Program.

Mr. Early: How are other, non-McKinney Act activities, to be carried out by CAPS if CSBG funding is eliminated?

Secretary Sullivan: Most Community Action Agencies receive funding from other Federal sources, such as the Social Services Block Grant and Head Start. These programs provide funds for both programmatic and administrative expenses. Funds provided under CSBG, account for only 12 percent or less of the Community Action Agencies' budgets. Furthermore, these agencies should be able to provide services on the same reimbursable basis as other providers and also leverage funds from local and State sources, especially the Community Action Agencies that have forged strong partnerships with public agencies and private organizations in their communities.

NIH DIRECTOR'S DISCRETIONARY FUND

Mr. Early: The budget request includes a proposal to allow the Director of NIH the authority to transfer up to one percent of all funds appropriated for NIH to high priority activities he may designate. Why is this transfer authority being proposed? Does this proposal reflect concerns about the adequacy of the NIH budget request? Doesn't the

Director have the opportunity to indicate and establish his or her priorities during the development of the budget request? Why didn't you request a special contingency account for the Director?

Secretary Sullivan: The request for the Office of the Director of NIH includes $20 million for the Director's Discretionary fund. In the event that $20 million is insufficient, the transfer authority will further the Director's ability to provide funds to address emerging priorities or sudden breakthroughs during the course of the fiscal year. Given the time lapse between budget formulation and implementation, and given the rapid progress made in certain health areas such as AIDS, circumstances may change sufficiently during the course of the fiscal year that warrant a change in the NIH spending priorities originally proposed.

We also believe the transfer authority will enhance the position of the Director. As you know, except for funds appropriated to the Office of the Director account, the NIH Director does not have direct control over the budget of the NIH. Providing the Director with more fiscal authority is one element we believe will broaden the scope of the Director's control over the enterprise and make this position more attractive.

AIDS TRANSFER AUTHORITY

Mr. Early: The budget also requests authority for the Secretary to transfer funds available for HIV activities between appropriation accounts. Why is this authority being requested?

Secretary Sullivan: This authority would provide the Department with a measure of flexibility to respond more quickly to unforeseen AIDS/HIV needs as they arise. Since AIDS is a very fast moving issue, scientific opportunities might arise in rare, but significant, instances that would best be addressed immediately, rather than waiting for the normal administrative and legislative budget channels to take action. The Congress allowed the Department this flexible authority in FYs 1988 and 1989, and I might point out it was necessary to utilize this authority twice in FY 1989, However, the Congress has prohibited its extension in FY 1990.

SECRETARY'S TRANSFER AUTHORITY

Mr. Early: The budget also requests a <u>third</u> transfer authority: authority to transfer such amounts as the Secretary determines, up to 3%, from

any PHS appropriation account to any account which includes funds available for HIV related activities. Why is this authority being requested, particularly since the Committee has declined to approve this proposal in the past?

Secretary Sullivan: This authority to allow the Secretary to transfer a limited amount of non-AIDS monies to AIDS activities is being requested for the same reasons as the other transfer proposal. Since we have no other mechanism, such as a discretionary contingency or reserve fund, this authority would allow the Department an additional means of flexibility to rapidly address unforeseen circumstances, such as breakthrough scientific opportunities.

Mr. Early: What is the maximum amount that could be transferred in FY 1991 given the budget request before us?

Secretary Sullivan: The potential maximum amount of total funds that could be transferred would be about $415 million. This represents 3% of the total PHS non-AIDS discretionary budget authority proposed for 1991.

Mr. Early: Mr. Secretary, why are you requesting all this transfer authority? Is this an indication that you have reservations about the adequacy of various aspects of the budget requests for the Public Health Service agencies?

Secretary Sullivan: We believe at this time that the $1.7 billion proposed is an appropriate spending level for AIDS/HIV activities in 1991. However, these transfer authorities have been requested to enable us to meet any unforeseen needs quickly, which is a responsible request to make when confronting a disease such as HIV.

Mr. Early: Mr. Secretary, aren't you, in effect, asking for the authority to "rewrite" the final FY 1991 appropriation bill as it pertains to the NIH and the Public Health Service?

Secretary Sullivan: No, we view this request for transfer authority as providing the Secretary with a limited degree of flexibility to act quickly to reallocate resources to AIDS/HIV efforts in order to rapidly take advantage of unforeseen, but very high priority, scientific opportunities related to the fight against this devastating disease. The Congress would be notified promptly, as was the case twice in FY 1989, if the Department expected to utilize any transfer authority.

LITHOTRIPSY

Mr. Dwyer: Mr. Secretary, as you know Medicare has placed greater emphasis on outpatient treatments and non-invasive procedures in recent years. One such "new" procedure is entitled renal lithotripsy, which uses shockwaves to smash kidney stones without surgery. There are three renal lithotripsy units in New Jersey, one set up by a consortium of doctors and two by a consortium of hospitals. A patient could be admitted to the hospital, transported to the lithotripsy unit for treatment, and returned to the admitting hospital for observation. Despite the cost savings of renal lithotripsy as well as its apparent health benefits, HCFA will not reimburse for this procedure under Medicare in New Jersey.

It is my understanding that a HCFA task force in Baltimore has been examining renal lithotripsy reimbursement for the past three years. Could you please tell me the status of their deliberations, and when can Medicare recipients expect reimbursement for this procedure?

Secretary Sullivan: We have no task force currently studying this issue. However, you may be referring to HCFA's recent deliberations on additions and deletions to the Ambulatory Surgical Center (ASC) list. Lithotripsy was recommended as an addition to this list. After reviewing requested public comments on the appropriateness of covering lithotripsy in an ASC setting, HCFA determined that outpatient utilization of lithotripsy may only be safe with a carefully selected patient population and will continue to be an inpatient hospital procedure for the majority of patients. We will, of course, review the appropriateness of lithotripsy as an ASC procedure in considering updates to the current list.

Mr. Dwyer: It is my understanding that renal lithotripsy is reimbursed in other states? If this is the case, why not in New Jersey?

Secretary Sullivan: Lithotripsy for kidney stones is covered under Medicare; however, this policy does not address the issue of the setting for the delivery of services (i.e., inpatient or outpatient). The choice of site is a judgment determination to be made by the patient's physician. However, when lithotripsy is performed in a freestanding facility payment of a facility fee or other type of special overhead /technical component payment is precluded. It would appear that the consortium arrangements currently existing in New Jersey are considered freestanding facilities for

Medicare payment purposes. I have, however, asked my staff in the Health Care Financing Administration to look into the details of the situation in New Jersey to be sure that payment is being made, where appropriate, for lithotripsy services.

The above delineated policy represents national Medicare policy on this issue. It would appear, therefore, that to the extent that lithotripsy is covered (and payment made) in other states, conditions similar to those in New Jersey are not present.

PEDIATRIC AIDS

Mr. Dwyer: Mr. Secretary, in the State of New Jersey, the typical AIDS sufferer is either a woman or a child. In all, women comprise 21% of the AIDS patients in New Jersey and children comprise 3%, higher than any other state. In addition, five metropolitan areas -- two of which, Middlesex and Monmouth Counties, are in my district -- are among the top 25 metropolitan areas with the highest incidence of pediatric AIDS.

As you know, only a percentage of the basic research in the adult manifestations of AIDS will be relevant to the pediatric population. In addition, many biomedical research issues are relevant only to the pediatric AIDS population. Mr. Secretary, could you tell us about current efforts to address the unique problems of pediatric AIDS?

Secretary Sullivan: Pediatric AIDS is a major focus of the increases requested for AIDS activities in 1991. HHS will spend about $172 million in 1991 directly on pediatric AIDS. This is an increase of +$35 million, or +26%, over 1990 and +$74 million, or +75%, over 1989. Our efforts in this area have been guided by the December 1988 recommendations of the HHS Work Group on Pediatric HIV Infection and Disease, which was chaired by Dr. Antonia Novello.

In the research area, NIH, CDC, and ADAMHA will spend about $118 million, or +14%, in 1991 for research on the efficacy of drug treatments in children and on the transmission of the HIV virus in children and women of childbearing age, and on improving surveillance of pediatric HIV cases. In 1989, NIH expanded its clinical trials network to include 15 pediatric units aimed specifically at treating children with HIV infection. In addition, 7 other centers which primarily study adults are also now evaluating drug treatments for HIV infection in children. In 1989, AZT, or zidovudine, was made available for use in treating children

under the age of 13 who have AIDS or advanced HIV infection. Under an FDA-approved treatment IND, the drug is being provided free of charge by the manufacturer to treat these children. Other clinical trials are studying various drug combinations for children with AIDS or ARC, and other studies are examining the effect of using AZT in both HIV-infected pregnant women and newborns.

In the social services area, the Office of Human Development Services (OHDS) expects to spend $17 million in 1991 for a wide range of demonstration projects that offer models for providing social services to HIV-infected children and their families. These projects include $6 million for a new initiative in 1991 to address the immediate non-medical needs of infants born to crack-cocaine using mothers and to increase access to comprehensive multi-disciplinary services. About $10 million will be spent to continue the prevention and services efforts of the Abandoned Infants Assistance program; and approximately $1 million will used for recruiting and supporting foster families for "boarder babies" with AIDS or HIV infection, coordinating medical and social services, and providing innovative child welfare services for HIV-infected children and their families.

In the area of health services and prevention, HRSA and CDC will spend over $37 million, and increase of $15 million or +66%, in 1991 on pediatric AIDS health care demonstrations and on projects in high incidence cities to prevent perinatal transmission of AIDS from HIV-infected mothers to their newborn children.

In addition, while not specifically directed to pediatric AIDS, the National Institute on Drug Abuse (NIDA) in ADAMHA will spend $63 million in 1991 on community-based outreach and prevention and treatment projects targeted to inner city youth, minorities and drug abusers which will indirectly effect pediatric AIDS. About 60% of all pediatric AIDS cases due to perinatal transmission occur in infants born to IV drug abusers or to women who are sexual partners of IV drug abusers.

Mr. Dwyer: Would you please discuss ongoing efforts to determine maternal-fetal transmission of the AIDS virus as well as an improvement in diagnostics?

Secretary Sullivan: The National Institute of Child Health and Human Development (NICHD) at NIH, in collaboration with the National Cancer Institute (NCI), has been conducting for three years a study

of maternal-child transmission of HIV infection. The study is attempting to determine the rate of transmission of infection from mother to child, as well as the factors affecting transmission. In addition, NICHD is collaborating with the National Institute of Allergy and Infectious Diseases (NIAID) in a multicenter, five-year study of maternal-child HIV transmission. This study will examine in depth the factors affecting transmission as well as the outcome of children infected with the virus.

In the area of diagnostics, pediatric AIDS presents a unique challenge. With many of the children born to infected mothers, we are still unable to differentiate between actual HIV infection in a child versus the presence of the mother's antibodies until the child is 16-18 months of age. In response to this problem, NICHD has recently awarded six research project grants to study the question of how to improve methods of early diagnosis of HIV infection in neonates, infants, and children.

Mr. Dwyer: How many HIV-infected children and adolescents currently participate in clinical trials for AIDS drugs, and what efforts are underway to increase the number of minority children in treatment protocols?

Secretary Sullivan: NIH is currently conducting 16 clinical trials for the study of a variety of therapeutic agents which may be useful in the treatment of HIV infection in children. So far, a total of 796 children have been enrolled in these clinical trials. This incudes eight trials in which a total of 564 children have been enrolled and additional children are being recruited; and eight other trials which have 232 children participating and enrollment has been completed.

NICHD has an impressive record with respect to involving minority children in clinical trials. For example, it is currently conducting a clinical trial involving 28 medical centers around the country, including a center in Puerto Rico. Of the 345 children enrolled in this trial, 87% are Black or Hispanic. Making clinical trials more accessible to minority families has involved devoting attention and resources to reducing barriers that prevent these families from participating in research protocols. To offer expanded access to minority children infected with HIV, NICHD plans to join these 28 medical centers with the pediatric AIDS Clinical Trials Units supported by NIAID.

FOSTER CARE AND ADOPTION

Mr. Hoyer: The Department has provided a $550 million increase for current Foster Care and Adoption services ($1.9 billion total), and a $47 million increase for Child Welfare Services ($300 million total), but do these funds target families that are dysfunctional because of substance abuse?

Secretary Sullivan: The Department has provided a $552 million increase for FY 1991 over FY 1990 for Foster Care and Adoption Assistance primarily because of the Department's expectation that the number of children and families entering the Child Welfare System will continue to grow at an alarming rate. In Foster Care, for example, the number of children eligible for the title IV-E maintenance payments program is expected to grow from an average monthly number of 177,000 in 1990 to over 205,000 children in 1991, a 16% increase. Although States do not currently submit data on the family problems necessitating the removal of children from their homes and placement in foster care, anecdotal information indicates that family crises resulting from substance abuse is the major factor in the dramatic increase in the number of children entering the foster care and child welfare systems. Therefor, although the increases in Foster Care, Adoption Assistance and Child Welfare Services are not targeted to families that are dysfunctional because of substance abuse, we do expect much of these increased funds will be used to serve these families entering the system because of problems related to substance abuse.

Mr. Hoyer: My understanding of the problem is that child abuse, neglect and abandonment by substance abusing parents has not replaced the other child protection problems, but has simply displaced them, and I'm wondering if you could support a more targeted effort to provide services to these children whose parents are drug abusers?

Secretary Sullivan: In addition to the significant increases requested for Payments to States for Foster Care, Adoption Assistance and Child Welfare Services, much of which will be used by States to serve children and families afflicted by substance abuse-related problems, the Department's FY 1991 budget provides support for targeted efforts to address the unique needs of children whose parents are drug abusers. The budget requests a $6 million increase for a new initiative to address the immediate non-medical needs of HIV-infected children and infants born to crack-cocaine using mothers. The budget also provides $10 million

for the Abandoned Infants Assistance program to continue support for demonstration projects that prevent the abandonment of infants by drug-abusing parents, including HIV-positive children, and to provide comprehensive services to those who are abandoned. In addition, States currently have the option to use the drug portion of the ADAMHA Block Grant (+$100 million in FY 1991) as well as treatment demonstration funds provided through the National Institute on Drug Abuse and the newly created Office for Treatment Improvement within the ADAMHA, to provide counseling for the entire family.

SSA SERVICE PROVISION

Mr. Hoyer: Mr. Secretary, I have been very interested in the level and adequacy of service provided by the Social Security Administration since the inception of the 800 number service. Will there be any changes in FY 91 in the number of personnel involved in providing direct public services?

Secretary Sullivan: The approval of SSA's budget as requested for fiscal year 1991, will permit SSA to devote as many full-time equivalents to direct service to the public in fiscal year 1991 as in fiscal year 1990. We will retain the same managerial flexibility in FY 91 which we have used in FY 90. For example, part time teleservice representatives (TSR) have been offered full time employment, additional TSR's have been hired, and overtime has been offered to TSR's. In addition, a new backup unit was established in Chicago in FY 90 to handle calls during peak call times. On a temporary basis, telephone lines were added to some field offices, and some "mini-teleservice centers" and State-wide answering units will remain open nation-wide.

Mr. Hoyer: Are you comfortable with the Social Security Administration's ability to adequately invest in the automation that sustains the 800 number service, while assuring that employees who respond to telephone inquiries are adequately trained and supervised?

Secretary SUllivan: Yes. SSA has provided every TSR with a personal computer terminal which provides direct access to all SSA's beneficiary records. SSA has contracted with MCI to furnish: needed phone lines, assistance in devising the most efficient call routing patterns, and comprehensive management information concerning the functioning of the system. SSA provides the same extensive

training on the rules and procedures of the Social Security program to TSRs as is provided to employees in field offices.

Mr. Hoyer: Can you tell the committee your plans with respect to expending the $50 million SSA contingency fund requested to help deal with unanticipated workloads?

Secretary Sullivan: The FY 91 budget request will fully fund all workloads anticipated at this time. The $50 million contingency reserve in LAE for FY 91 is for unanticipated workloads, and as such, we would not expect to use it.

CHILD SUPPORT ENFORCEMENT

Mr. Hoyer: Dr. Sullivan, could you elaborate on the Administration's proposals to cap the Federal funds available for administering Child Support Enforcement programs for AFDC families and for requiring Food Stamp recipients to cooperate in collecting child support in order to maintain eligibility for Federal aid?

Secretary Sullivan: These two proposals are designed to encourage States to provide child support services more efficiently and to increase the incomes of families receiving different types of public assistance by insuring that they receive child support enforcement services where appropriate.

The first proposal would limit Federal funds available for reimbursement of State administrative expenses. Affected States would be those that do not operate efficiently. Capping the Federal match will stimulate these States to increase their collections and to become more efficient.

Beginning in FY 1991 for States that are not effective, that is, do not collect a dollar on behalf of AFDC families for each Federal dollar spent on administrative costs, the amount of Federal funding for State administrative costs would be capped at an amount equal to the State's total child support collections on behalf of AFDC families. In FY 1989, funds for eight States would have been capped under this proposal. The Federal funding limit for States that continue not to meet the effectiveness criterion would be phased down from 100 percent of AFDC collections in FY 1991 to 66 percent in FY 1999. This proposal is projected to save $10 million in FY 1991.

The second proposal would provide general legislative authority under which recipients of other Federal benefit programs could be required to cooperate in the establishment of paternity and child support enforcement as a condition for their continued receipt of Federal Assistance.

This proposal would make child support available to an expanded number of families not now receiving it. For example, the Food Stamp program is envisioned as one of the first programs affected: of the estimated 250,000 Food Stamp-only families which would be referred to the Child Support Enforcement program, child support payments would be collected on behalf of approximately 125,000 families. This proposal is expected to increase Child Support Enforcement costs by $30 million in FY 1991; however, in Food Stamps, the initial program likely to be affected by this proposal, these costs would be offset by savings to the Food Stamp program projected at $50 million in FY 1991.

Mr. Hoyer: Do you believe that Federal legislation making the failure to pay court ordered child support a Federal crime would be beneficial?

Secretary Sullivan: At this time, we do not have the information to determine if it would be useful to have a law which would make failure to pay child support a Federal crime. It is worth noting that most States already have criminal statutes on their books, as child desertion leading to public dependency has long been considered a crime in many States. In addition, the trend in recent years has been towards handling failure to pay as a civil matter, rather than as a criminal matter.

LOW INCOME HOME ENERGY ASSISTANCE PROGRAM

Mr. Hoyer: At least 17 Governors, including Maryland's Governor Schaeffer, contacted President Bush to seek additional funding for LIHEAP. The Administration proposes a cut of $343 million in the LIHEAP Program. Can the Department provide any specific rationale with respect to how you arrived at the $343 million figure?

Mr Secretary: Given the broad variation in energy assistance needs, the Department believes it is appropriate for the energy assistance needs of low-income households to be funded not only by Federal resources, but also by State and local funds. That is, individual States could be taking a more expansive role in meeting the energy needs in their respective jurisdictions. We therefore propose a 25% reduction in FY 1991. The Governors

of five of those States -- including Maryland -- continue to divert LIHEAP funds into other programs. Adjusted for inflation, heating prices have declined continually, with this year being a temporary aberration. We believe Federal appropriations should reflect this long-term decline in heating costs.

HEAD START

Mr. Hoyer: The Budget Proposal includes a 36% or $500 million increase for the Head Start Program. I wish the President had proposed a budget that would have reached 100% of the eligible disadvantaged pre-school-aged children. How many and what percentage of eligible children does the Department project will be able to participate in the program as a result of the requested increase?

Secretary Sullivan: Up to an additional 180,000 children will participate in Head Start in 1991, bringing the total number of children to 668,470. The President's goal for Head Start is to provide at least one year Head Start to all low-income children before they enter kindergarten. Given the availability of kindergarten in all 50 States, most children will participate in Head Start when they are four years old. The 1991 request could allow up to 70 percent of low-income children to receive benefits of a Head Start experience in the year before they enter kindergarten.

Mr. Hoyer: What age levels are eligible to participate in Head Start?

Secretary Sullivan: The Head Start Act allows funding of Head Start programs which are "...focused primarily upon the children from low-income families who have not reached the age of compulsory school attendance..." Most Head Start programs serve children who are 3 - 5 years old, with Migrant programs and Parent Child Centers serving a limited number of children younger than three years old.

Mr. Hoyer: If the Administration projects that 60% of eligible 4-year olds could participate under the President's request, what percentage of the entire eligible population could participate under the President's request?

Secretary Sullivan: With the $1.9 billion requested in 1991, up to 70 percent of low-income children could be served by Head Start in the year before they enter kindergarten. This is somewhat different than serving 60% of four year olds since a small portion of those children being served by Head

Start in the year before they enter kindergarten will be older than four.

Currently there are an estimated 2,475,000 low income three, four and five year olds. The 1991 President's budget request will enable Head Start to serve 622,000 of these children, or 25%. The remaining 66,000 children being served by Head Start are either less than three years of age, or from families with incomes above the poverty line.

However, it is estimated that all but a small portion of five year olds are enrolled in Kindergarten and, consequently, five year olds should not be considered as part of Head Start's target population. Thus Head Start considers its primary population as low-income three and four year olds. In FY 1991, there will be an estimated 1,650,000 low-income three and four year olds. The President's budget request would allow Head Start to serve 588,000 of these children, or 35.6% of the low-income three and four year old population. The remaining 80,000 children being served by Head Start in FY 1991 will be under three years of age, over four years of age, or from families with incomes above the poverty line.

Mr. Hoyer: Could you provide for the record the number of eligible children by age group from 1980 to 1991? Could you provide a table or tables that indicate the level of participation by age group in the program from 1980 to 1991?

Secretary Sullivan: The following table provides the requested information on income-eligible and participating children by age group.

HEAD START

Children From Low-Income Families: Numbers Eligible and Participating in Head Start, 1980 - 1991

	3 Year Olds			4 Year Olds			5 Year Olds			Total, 3-5		
FY	Low-Inc. Eligible	Low-Inc. Partic.	Percent Partic.	Low-Inc. Eligible	Low-Inc. Partic.	Percent Partic.	Low-Inc. Eligible	Low-Inc. Partic.	Percent Partic.	Low-Inc. Eligible	Low-Inc. Partic.	Percent Partic.
1980	599,000	79,298	13.24%	599,000	196,616	32.82%	599,000	75,072	12.53%	1,797,000	350,986	19.53%
1981	686,333	88,417	12.88%	686,333	198,684	28.95%	686,333	73,589	10.72%	2,059,000	360,690	17.52%
1982	773,667	91,763	11.86%	773,667	206,806	26.73%	773,667	63,922	8.26%	2,321,000	362,491	15.62%
1983	861,000	104,493	12.14%	861,000	216,812	25.18%	861,000	67,014	7.78%	2,583,000	388,319	15.03%
1984	845,500	109,209	12.92%	845,500	235,218	27.82%	845,500	67,205	7.95%	2,536,500	411,632	16.23%
1985	830,000	107,369	12.94%	830,000	244,801	29.49%	830,000	68,716	8.28%	2,490,000	420,886	16.90%
1986	815,000	107,286	13.16%	815,000	248,904	30.54%	815,000	64,372	7.90%	2,445,000	420,562	17.20%
1987	818,333	110,291	13.48%	818,333	250,276	30.58%	818,333	55,146	6.74%	2,455,000	415,713	16.93%
1988	821,667	97,989	11.93%	821,667	268,406	32.67%	821,667	46,865	5.70%	2,465,000	413,260	16.77%
1989	825,000	107,106	12.98%	825,000	274,910	33.32%	825,000	34,274	4.15%	2,475,000	416,290	16.82%
1990	825,000	107,106	12.98%	825,000	309,815	37.55%	825,000	34,274	4.15%	2,475,000	451,195	18.23%
1991	825,000	107,106	12.98%	825,000	480,815	58.28%	825,000	34,274	4.15%	2,475,000	622,195	25.14%

Notes: 1. Numbers of income-eligible children are based on best available census data and representative estimates where appropriate.

2. Approximately 5% of Head Start participants are not from low-income families, but can otherwise benefit from the Head Start experience. Although these children are allowed to participate according to the Head Start Act, they do not figure into calculations of percent of eligibles served because they are not "income-eligible." Estimating children from low-income families is the only means of defining the Head Start eligible population.

HEAD START

Mr. Hoyer: How much would it cost to achieve full participation of every eligible child in FY 1991?

Secretary Sullivan: An estimated 20% of Head Start eligible children have alternative services available to them, such as State-funded preschool or child care by a relative, or their parents elect to keep them at home, and consequently would not participate in Head Start. Thus if we are able to provide a Head Start experience to 80% of the estimated 825,000 low-income children entering kindergarten each year, in the year before they enter kindergarten (primarily four-year olds), we will have achieved universal Head Start. To do this will require an increase of approximately $500 million.

Mr. Hoyer: Can you provide projected funding increases for the next three fiscal years that would achieve 100% participation of all eligible children by 1993?

Secretary Sullivan: To serve all (80% of) low-income children for at least one year by 1993, it is estimated that we would need the $500 million already requested in 1991, $250 million in 1992, and another $250 million in 1993.

INJURY PREVENTION

Mr. Hoyer: The problems of premature death and injury in the young and minority communities is severe. More than half the children who die because of injury in Maryland are African Americans. In Maryland, African American children die in house fires at twice the rate of white children. The area of injury prevention is an important component of the CDC which is extremely relevant to the national agenda in terms of minority health promotion, and health care cost reduction. Could you comment on this area of the Department's mission, and whether you believe it would be a higher priority if the resources were available?

Secretary Sullivan: The 1991 budget includes $22.6 million for CDC activities related to injury control. This maintains the expanded program level resulting from the 1990 Congressional appropriation, and represents a 7.9% increase over 1989. These funds will be used to continue support of seven Injury Prevention Research Centers; 40 individual extramural investigators conducting applied research

in injury prevention and control; seven State or local health agencies conducting injury surveillance; six State or local health agencies implementing targeted injury control interventions; and 15 State or local health agencies building the capacity to support injury control activities. In addition, CDC supports intramural injury prevention research and provides technical assistance to State and local health agencies. States also have the flexibility to use funds from the Preventive Health Services Block Grant to support injury control projects if the State regards such activities as high priorities.

ONE STOP SHOPPING

Mr. Hoyer: Mr. Secretary, could you explain the difference in concept and detail between the proposed "One Stop Shopping" program associated with the Maternal and Child Health Program and the Comprehensive Child Development Centers funded under the Office of Human Development Services?

Secretary Sullivan: The proposed "One Stop Shopping" initiative will provide $25 million to States and communities, through the established Maternal and Child Health Block Grant system, to better coordinate health and social services for low-income mothers and children at the community level. These funds will go out by formula to States, to be used by States to establish their own coordinated systems so that mothers and children can have one point of access for a variety of services.

The Comprehensive Child Development Services Centers funded through the Office of Human Development Services is a discretionary grants program. The Office of Human Development Services directly funds 22 centers which provide intensive, comprehensive, integrated and continuous supportive services for low-income children from birth until they reach public school age.

SOCIAL SECURITY ADMINISTRATION

Mr. Porter: Mr. Secretary, I am very concerned about the future unfunded obligations of the Social Security Trust. Congress is continuing to act irresponsibly by counting Social Security reserves against the budget deficit for the purposes of Gramm-Rudman -- in effect, we are covering up the true size of the deficit.

I believe that a more responsible plan is to refund accumulated reserves to individuals in the form of contributions to Individual Social Security Retirement Accounts (ISSRAs). Such a plan would have the effect of creating a $3 trillion savings base over the next thirty years, while reducing future demands on the trust. At the same time, it would keep the Social Security reserves out of the hands of Congress. Would you comment on this approach?

Secretary Sullivan: I remain firmly opposed to any proposal which breaks faith with the 1983 Bi-partisan agreement on Social Security. I am deeply committed to maintaining the integrity of the Social Security System and insure that there are ample funds to pay full benefits now and in the future.

HEALTH CARE

Mr. Porter: You have already discussed the budget deficit and its effect on your spending priorities. I would like to take a longer look at our budget situation.

Rising health care costs are the most serious obstacle to long-term budget stability. Some projections show that Medicare and Medicaid outlays will exceed outlays for old age benefit payments sometime early in the next century. Clearly, under our current system of price administration on both the hospital and physician sides, Congress cannot continue to make budget-driven cuts in the inflation updates, and at the same time expect to retain the same high quality of care.

What long term reforms can we make to our health care delivery system to meet the twin goals of high quality and cost containment?

Secretary Sullivan: There are a number of groups making comprehensive studies of our health care system at the present time. The Pepper Commission, the Social Security Advisory Council, and my Undersecretary's Work Group will all be

making recommendations. The President has directed me to conduct a Domestic Policy Council assessment of these recommendations.

In the meantime, there are several major steps that are being taken to restructure the delivery and payment for health care under Medicare. The physician payment reform enacted last year and the managed care initiatives in this year's budget will shift the emphasis in treatment to more primary and better managed care. This will not only provide better quality of care, but should in the longer term significantly reduce the spiraling rate of growth in the cost of that care.

FAMILY PLANNING

Mr. Porter: The press has focused a great deal of attention on AIDS babies and children. Since most of these victims contracted the disease perinatally, shouldn't we do more to ensure that sexually active young people have access to family planning services?

Secretary Sullivan: The Adolescent Family Life program is directed specifically to the complex issues and problems of early adolescent sexual activity and adolescent pregnancy and parenting. This $9.4 million program provides a full complement of education, counseling, and services targeted to teens, including family planning services. Family planning services are also available to minors with the permission of a parent through the $139 million Family Planning program.

Mr. Porter: This Administration opposes abortion. In light of this fact, doesn't it make sense to focus more resources and attention on Title X, a program which prevents abortion?

Secretary Sullivan: We believe the budget of $139 million requested for the Family Planning program in 1991 is substantial, but only part of the total Federal funds available for family planning. Medicaid provides the major support for low-income women to receive family planning services. In 1991, we project that $292 million, an increase of $18 million over 1990, will be reimbursed by the Federal government for a variety of family services to the most in need populations.

Mr. Porter: You haven't conducted any Title X data collection and analysis since 1983. When do you intend to carry out the plan you presented to Congress for such a program?

Secretary Sullivan: The Department annually performs a National Survey of Family Growth which samples approximately 8,000 people regarding issues of pregnancy, childbirth, contraception, family planning and other related topics. We believe this survey, although not specific to Title X, is an excellent source of information regarding these important policy issues. In 1990, we plan to begin collecting information specifically on Title X clinic users. These data are available through public use data tapes and a series of papers published by the National Center for Health Statistics.

In addition, HRSA collects data on the Title X program which includes patient counts, or number served, and characteristics of the population including income and age status. These data are collected through the Bureau of Health Care Delivery and Assistance Common Reporting Requirements.

CONTRACEPTION

Mr. Porter: We have too many abortions in this country. We also have a very serious problem with AIDS which you have stressed and which is reflected in your budget request. But at the same time, our country is getting out of the contraceptive development business largely because of the liability situation. Given the tremendous need, shouldn't we place a greater emphasis on contraceptive development at the NICHD?

Secretary Sullivan: I agree that the problems of AIDS and other sexually transmitted diseases as well as unwanted pregnancies warrant further research into means of reducing risky sexual activity. Contraceptive development is one method which may allow us to better control these problems. The National Institute on Child Health and Human Development (NICHD) devotes a significant amount of attention to contraceptive development. The FY 1991 request for NICHD includes $133 million for the Institute's Center for Population Research which supports research in contraceptive development and evaluation as well as studies on fertility and sexual behavior.

NIH

Mr. Porter: You referred earlier to NIH as the crown jewel of HHS. I would certainly agree with that characterization. But NIH continues to suffer from under-budgeting. Once again, you bring before us an essentially flat funding request for NIH.

You noted earlier that NIH funds only 25% of all approved grant requests. Salaries are pitifully low, and you haven't filled a senior position at NIH from outside in 10 years. Discouraged researchers leave the field, and more importantly, very few new researchers are entering the field. We aren't following up hot leads.

We spend $60 billion on defense research and development, and less than $8 billion on NIH. Aren't these priorities out of whack?

Secretary Sullivan: As Secretary of Health and Human Services I do not feel its is appropriate for me to pass judgement on the budget for the Department of Defense. I can assure you, however, that the budget request for the National Institutes of Health will allow us to continue to make significant progress in preventing and combatting a variety of diseases that plague our society.

The 1991 request for NIH provides an overall increase of 4.7 percent over the 1990 level. This rate of increase exceeds the projected rate of inflation of 4.2 percent. Overall support for NIH basic research in 1991 increases by 5.7 percent. Those research mechanisms which primarily support basic research were provided increases which exceed the inflation rate: +5.4 percent for research project grants; +5.5 percent for research centers; and +6.9 percent for intramural research. Areas of utmost importance, for example the Human Genome Initiative (+81.5 percent) and AIDS (+7.6 percent) will receive significant increases.

REFUGEE RESETTLEMENT

Mr. Porter: As with too many programs, refugee resettlement is one where the Federal government is breaking its bargain with the States. The States are now picking up most of the costs, and I don't think the day is far away when States stop agreeing to resettle these people. Similarly, voluntary resettlement agencies are being stuck with more than their fair share of the resettlement costs. Refugee numbers keep going up, and yet you've proposed to level fund refugee programs. Why?

Secretary Sullivan: For FY 1991, we propose the same funding level, $369 million, that was provided for in the FY 1990 appropriations act and the projected refugee ceiling is 1,000 less than in FY 1990. The voluntary resettlement agencies received in FY 1990 the largest grant award in the history of the program, $40 million - the same funding level proposed for FY 1991. Most refugee

resettlement funds subsidized the States' share of public assistance programs. The Federal government already pays the majority of those costs through entitlement accounts.

Mr. Porter: Are these your numbers or Mr. Darman's?

Secretary Sullivan: The proposed funding level of $368 million for refugee assistance in FY 1991 represents the Administration's request.

SMOKING

Mr. Porter: Dr. Sullivan, I commend you for your recent campaign against a cigarette marketed to blacks. You provided a true service to this country. But I am concerned that we should look at the smoking issue more broadly. I had hoped, frankly, that you would do more to address smoking and its attendant health risks to smokers and non-smokers alike, in a more general fashion. Do you plan to follow up with a more general effort to reduce preventable, smoking-related mortalities in this country?

Secretary Sullivan: Cigarette smoking is clearly the single most preventable cause of premature death and disability in this country. While smoking has declined significantly since the first Surgeon General's report in 1964, 29%, or nearly one-third, of all adults in the U.S. continue to smoke. The American Cancer Society estimates that approximately 390,000 Americans died in 1989 from smoking-related diseases. This represents about one out of every six deaths in the United States. Lung cancer has now replaced breast cancer as the leading cause of cancer death among women. Smoking-related diseases also cost the nation more than $52 billion annually. This averages out to a national annual cost of $221 per person, which all of us, smokers and non-smokers alike, pay for largely through increased health care and insurance costs.

In the face of such distressing statistics, I can assure you that I am deeply committed to reducing preventable smoking-related illnesses and deaths for all Americans. However, cigarette smoking is clearly more common among minority groups. For example, 32% of Hispanic men and 42% of Black men smoke, compared to 31% of white males. The resulting disproportionate impact of smoking-related health problems in minorities and the poor cannot be denied.

In the 1991 budget request, we are requesting approximately $85 million throughout PHS for smoking and health activities. This includes about $80 million on biomedical and behavioral research to further our understanding of smoking's destructive effects on health. The National Cancer Institute (NCI), for instance, is studying various methods of modifying smoking behaviors, and supports a number of major clinical trials to evaluate the effectiveness of smoking cessation programs. About $1.1 million of CDC's proposed $11.5 million Infant Mortality Initiative in 1991 will focus on increasing support to smoking cessation programs for low-income pregnant women. Smoking is a major risk factor for low birth-weight in infants. Also, within CDC, the Office of Smoking and Health is supported at about $3.4 million per year to coordinate the Department's anti-smoking activities, and to maintain a national information clearinghouse to respond to public inquiries on smoking prevention.

ABANDONED INFANTS ASSISTANCE ACT

Mr. Young: Mr. Secretary, many Americans, including President and Mrs. Bush, have expressed concern about the innocent victims of drug-abuse and AIDS -- infants and very young children. It is simply a heart wrenching experience to see and hold these babies who through no fault of their own are born addicted to drugs and infected with the deadly AIDS virus. Too many times, the parents of these children abandon them in the hospital or for one reason or another cannot care for them at home. In response to our concern, this Committee last year appropriated $10 million to implement the Abandoned Infants Assistance Act to find a way to care for these children. Who is the lead agency within your Department for this program and how are these funds being administered?

Secretary Sullivan: The Administration for Children, Youth and Families within the Office of Human Development Services is planning publication of funds availability in the Federal Register in early Spring, and grants are expected to be made in September. Grants will provide financial support to public and non-profit private entities to develop, implement and operate demonstration projects that will prevent the abandonment of infants and young children; identify and address their needs; assist such childre to reside with their natural families or in foster care, as appropriate; provide respite care for families and caregivers; and recruit and train caregivers.

Mr. Young: In appropriating these funds last year, our Committee directed that the Office of Human Development Services should work closely with the Health Resources and Services Administration which oversees the pediatric AIDS health care demonstration grant program in coordinating the Abandoned Infants Assistance Act. What steps has the Department taken to ensure this coordination between agencies takes place?

Secretary Sullivan: Officials from the Administration for Children, Youth and Families (ACYF), have already met with officials from both the Bureau of Maternal and Child Health within the Health Resources and Services Administration (HRSA), and the Administration on Developmental Disabilities, and future meetings are planned. Coordination is taking place between ACYF and HRSA concerning the Federal Register Grants announcement, and coordination will continue when grant applications are received and funding decisions are being made.

SLIAG

Mr. Young: Mr. Secretary, of great concern to the State of Florida is the action taken last year and the budget request for Fiscal Year 1991 for the State Legalization Impact Assistance Grants (SLIAG). In your justification statement, where the allocation for this program is reduced by almost $700 million, you cite the slow spend out rate of this program. When Congress instituted this program, it fully anticipated a slow spend out rate. In fact, the program allowed the $4 billion that would be appropriated to the States over four years to be spent over a seven year period. The State of Florida has budgeted and fully anticipates needing its full share of these funds over seven year period ending in Fiscal Year 1994.

While there may be good reason to defer appropriating the full $1 billion that is authorized for this program in Fiscal Year 1991 because of the slow spend out rate, I would like to know your thoughts on possibly deferring some of these funds until the out years during which the States most heavily impacted by these newly legalized aliens anticipate the greatest need.

Secretary Sullivan: Based on the most current data available as well as recommendations by the Office of Inspector General to suspend the FY 1991 appropriations, we believe that the over $2 billion that will have been obligated to the States by FY 1991 will prove to be sufficient for enabling these long-term workers to finish integrating themselves into American society. By the end of FY 1991, most eligible legalized aliens will have been living and working in the United States for over 10 years, and will have completed all required Civics and English classes. They are much more likely to be working than the average citizen. As a result, we do not understand the basis of any claims that future costs will be too high. I would also point out that recent report completed by the Office of Inspector General, on February 14, recommends that the Department request to Congress the suspension of the FY 1991 $1 billion appropriation due to an overestimate of expenditures.

RURAL HEALTH

Mr. Weber: The President's budget proposes a Medicare update in the amount of 4.1 percent, which represents a real cut in Medicare. However, the President also expressed a willingness to consider different updates for urban and rural hospitals within that 4.1 percent. What are the Secretary's views on a higher update for rurals, thus further closing the urban/rural reimbursement gap?

Secretary Sullivan: I am very concerned about maintaining access to health care for rural Americans. For this reason, in 1990, I recommended and the Congress enacted a higher payment update for rural hospitals. In 1991 I expect to work closely with Congress to develop suitable adjustments in the update to account for the varying situations of rural, inner city, and other hospitals.

Mr. Weber: Last summer, Inspector General Kusserow issued a report which argued that rural hospitals are losing money because they have higher costs per patient. His proposed solution to the financial difficulties facing rural hospitals is to cut costs. Many of us have argued for some time that the unique geographic and demographic characteristics of rural hospitals necessarily forced them to have higher costs per patient and therefore, they deserve higher reimbursement rates. What are the Secretary's views on this debate?

Secretary Sullivan: The Department recommended and OBRA 89 enacted a higher PPS update for rural hospitals in FY 1990. The Department's 1990 PPS regulation also contained provisions to assist sole community hospitals and requested comments on how to improve existing policies. In addition, the Department, as directed by Congress, will be developing its recommendations on, and analyzing the impact of, using a single standardized rate on various groups of hospitals. We expect our report will be forwarded to Congress by October 1, 1990.

ANIMAL RIGHTS ACTIVISTS

Mr. Weber: Animal rights activists have engaged in extraordinary acts of vandalism and "terrorist" activities in recent years. Do you have any concerns about the growing menace of animal rights activists? What will you do to address these concerns?

Secretary Sullivan: We are very concerned about the damage and intimidation some activists have wrought on some sectors of the research community. We know of at least 71 instances over the past eight years in which animal rights activists have turned to criminal acts -- including bomb threats, theft, arson -- to protest the use of animals in research.

We recognize the need to better inform the public about how animals are used and for what purposes. We also believe that the animal rights activists have to a great extent exacerbated this problem. Consequently, we are working with the research community to develop ways to better educate the public about the need for using animals in research. At the same time, we appreciate the continued support of the Congress on this issue.

Mr. Weber: In light of the growing fiscal pressures on biomedical research, do you have any dollar estimates as to the amount of damage that has been done to research by animal rights activists?

Secretary Sullivan: The destruction of property and the possibility of danger for research personnel are exacting a high cost on the research community, both in fiscal and psychological terms. No one has yet to total the actual dollar value of the acts of destruction and vandalism already undertaken, however, through anecdotal information the Public Health Service has a sense of the cost of the problem. In just 4 of the 71 cases of animal rights vandalism reported to the Public health Service, damage totaled $5 million. This is clearly a price we ultimately can not pay.

Mr. Weber: Do you have any estimates as to how much progress in biomedical research has been set back by animal rights activities?

Secretary Sullivan: At this time, we do not have any firm estimates on the cost of research setbacks attributable to animal rights protest activities. However, scientists are reporting to us a reluctance to pursue research in certain areas that require the use of animals because of the heightened attention animal rights activists generate, and because the scientists are increasingly unwilling to engage in an extensive dialogue about the appropriateness of using animals in scientific experiments.

COMMUNITY VALUES

Mr. Weber: Last year you mentioned to a group of my colleagues that a way must be found to impart certain values to the underclass. Can you elaborate on this idea?

Secretary Sullivan: The point that I was trying to make applies to all Americans. Simply put, I believe that many of the problems plaguing our communities today--high infant mortality rates, drug abuse, diseases like AIDS, and teen pregnancy--result in part from the erosion of values like family, community, and personal responsibility. As Americans, I believe that we have the power to solve many of these problems by returning to fundamental cultural values and traditional beliefs, by recapturing our spirit of family and by cultivating within our communities a new ethic of personal responsibility. Specifically, we need to emphasize a new culture of character for all Americans that strengthens personal qualities like moderation, perseverance, self-discipline, and service and in the process prepares the way to health, achievement, and fulfillment.

HEAD START

Mr. Weber: How does your agency want to spend the additional $500 million the President has authorized for the Head Start program?

Secretary Sullivan: The $500 million, or 36%, increase provided for Head Start is the largest single funding increase in the history of the program. The request signifies the Administration's commitment to making the Head Start experience available to all disadvantaged children to afford them an equal start in life. The 1991 budget request will: serve up to 180,000 additional children over FY 1990, bringing the total number of children served to 668,000; bring us closer to making universal Head Start a reality, especially if States join the President by dedicating State funds to local Head Start programs. This could enable us to serve up to 70 percent of all low-income children in the year before they enter kindergarten.

Mr. Weber: What are the issues being considered for the reauthorization of Head Start?

Secretary Sullivan: Since the Head Start program has been so successful in giving disadvantaged children and their families a better

start in life, we are not considering any major legislative changes. The Administration will propose legislation which will increase the 1991 authorization level to $1,886 million, consistent with the President's budget request. In addition, some minor amendments are being considered, like strengthening Head Start's coordination provision so that grantees will be directed to coordinate Head Start with public pre-school programs, as well as agencies administering the State's JOBS program. Finally, to help maintain program quality, we are also adding a requirement that each program receive a comprehensive monitoring review at least once every three years.

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HEALTH CARE FINANCING ADMINISTRATION

ABORTIONS

Part I - Background

HHS's Appropriations Acts have contained restrictions on the Department's funding of abortions since the Appropriations Act for FY 1977. HHS was enjoined by a Federal District Court from enforcing the FY 1977 restrictions until August 4, 1977. Consequently, the Department provided funding for all abortions which were covered under a State's plan that were performed through that date. The appropriations restrictions, commonly known as the Hyde Amendment restrictions, have governed HHS's funding of all abortions performed after August 4, 1977, except for those abortions performed during the period February 19, 1980, through September 19, 1980. Federal funding was available for all medically necessary abortions performed during that period under the criteria set forth by the District Court for the Eastern District of New York in Harris v. McRae, 448 U.S. 297 (1980).

The following excerpts from instructions issued by HHS set forth the rules under which the Department has funded abortions performed after August 4, 1977, with its appropriations for FY 1977 through FY 1980.

1. For abortions performed after August 4, 1977, and for which funds appropriated by the appropriations act for FY 1977 or the continuing resolutions which appropriated funds through December 1, 1977, are used to pay the claim:

   "... where the attending physician, based on his or her professional judgment, has certified in writing that the abortion is necessary because the life of the mother would be endangered if the fetus were carried to term."

2. For abortions performed after August 4, 1977, and prior to February 14, 1978, and for which funds appropriated by P.L. 95-205 (appropriations act for FY 1978) or P.L. 95-480 (appropriations act for FY 1979) are used to pay the claim:

   (a) Where the attending physician, based on his or her professional judgment, has certified in writing that the abortion is necessary because the life of the mother would be endangered if the fetus were carried to term;

   (b) where two physicians, based on their professional judgment, have certified in writing that severe and long-lasting physical health damage to the mother would result if the pregnancy were carried to term; or

(c) for the victims of rape or incest, when such rape or incest has been reported promptly to a law enforcement agency or public health service.

The Department will accept any reasonable interpretation of those provisions for abortions covered under paragraph 2.

3. For abortions performed on or after February 14, 1978, and prior to August 21, 1978, and for which funds appropriated by P.L. 95-205 or P.L. 95-480 are used to pay the claim:

(a) where a physician has found, and so certified in writing to the State agency, that on the basis of his or her professional judgment, the life of the mother would be endangered if the fetus were carried to term;

(b) where two physicians have found, and both certified in writing to the State agency, that on the basis of their professional judgment, severe and long-lasting physical health damage to the mother would result if the pregnancy were carried to term; or

(c) for the victims of rape or incest, if the State agency has received signed documentation from a law enforcement agency or public health service stating that:

(i) the person upon whom the medical procedure was performed was reported, within sixty (60) days of the incident, to have been the victim of an incident of rape or incest; and

(ii) the report included the name, address, and signature of the person who reported the rape or incest.

4. For abortions performed on or after August 21, 1978, and for which funds appropriated by P.L. 95-205 or P.L. 95-408 are used to pay the claim:

(a) where a physician has found, and certified in writing to the State agency, that on the basis of his or her professional judgment, the life of the mother would be endangered if the fetus were carried to term. The certification must contain the name and address of the patient;

(b) where two physicians have found, and certified in writing to the State agency, that on the basis of their professional judgment, severe and long-lasting physical health damage to the mother would result if the pregnancy were carried to term. The certification must contain the name and address of the patient. At least one of the two physicians must also certify that he or she is not an "interested physician." An "interested physician" is one:

(i) whose income is directly or indirectly affected by the fee paid for the performance of the abortion; or

(ii) who is the spouse of, or another relative who lives with, a physician whose income is directly or indirectly affected by the fee paid for the performance of the abortion; or

(c) for the victims of rape or incest, if the State agency has received signed documentation from a law enforcement agency or public health service stating:

(i) that the person upon whom the medical procedure was performed was reported to have been the victim of an incident of rape or incest;

(ii) the date of the incident;

(iii) the date of the report, which must be within sixty (60) days of the incident;

(iv) the name and address of the victim and the name and address of the person making the report (if different from the victim); and

(v) that the report included the signature of the individual who reported the incident.

The continuing resolutions which made funds available for FY 1980, P.L. 96-86 signed October 12, 1979, and P.L. 96-123 signed November 20, 1979, removed the exception which allowed payment for abortions in those instances where severe and long-lasting physical health damage to the mother would result if the pregnancy were carried to term when so determined by two physicians. Thus, Federal funding for abortions was prohibited except: (1) where the life of the mother would be endangered if the fetus were carried to term; and (2) for

such medical procedures necessary for victims of rape or incest, when such rape or incest has been reported promptly to a law enforcement agency or public health service. Regulations implementing P.L. 96-86 were published at 42 CFR Part 441, on October 26, 1979. These regulations also applied to expenditures for abortions under P.L. 96-123 because the provision in that act governing abortions was similar to the one contained in P.L. 96-86.

On January 15, 1980, the District Court for the Eastern District of New York declared the Hyde Amendment unconstitutional insofar as it precluded payments for medically necessary abortions. That decision became effective on February 19, 1980, when the Supreme Court refused to extend a stay of the district court order. Federal funding then became available for all medically necessary abortions performed on or after February 19. The Supreme Court decision of June 30, 1980, reversed the district court's decision on the constitutionality of the Hyde Amendment. The petition for rehearing filed by the plaintiffs in the McRae case delayed the effective date of the Supreme Court's decision, leaving the district court order on payments for abortions in effect. The Supreme Court denied the appellee's petition for a rehearing in the McRae case on September 17, 1980, and the district court's order was vacated on September 19, 1980. Therefore, the availability of Federal funding for abortions performed after September 19, 1980, was subject to the FY 1980 Hyde Amendment restrictions; i.e., Federal funds under Medicaid were available only for abortions performed in life endangering circumstances and abortions performed in instances of promptly reported rape or incest.

On October 1, 1980, the President signed a joint resolution making continuing appropriations available for FY 1981 through December 15 or until the enactment of a subsequent appropriation. This resolution contained language which changed the conditions under which Federal funding was available for abortions under Medicaid. During FY 1980, Federal funds were available for abortions necessary for the victims of rape or incest when the rape or incest was reported to a law enforcement agency or public health service within sixty days. Under the FY 1981 resolution, Federal funds were available for abortions necessary for the victims of rape when the rape had been reported within seventy-two hours to a law enforcement agency or public health service. Federal funds were also available for abortions necessary for the victims of incest. There was no longer a reporting requirement for victims of incest. In cases of incest, Federal funding was available when the State agency had received a physician's written statement that the physician had been informed that the patient was a victim of incest. As in FY 1980, Federal funds continued to be available for abortions where the life of the woman would be endangered if the fetus were carried to term.

On June 5, 1981, the President signed the Supplemental Appropriations and Rescission Act, 1981. Under this act, FFP is no longer available for abortion claims paid after June 5, 1981, for victims of rape or incest. Federal funds continue to be available for abortions where the life of the mother would be endangered if the fetus were carried to term.

Subsequent Congressional measures have continued to make Federal funds available for abortions where the life of the woman would be endangered if the fetus were carried to term. See P.L. Nos. 97-51, 97-92, 97-276, 97-377, 98-107, 98-139, 98-619, 99-107, 99-154, 99-434, 99-464, 99-465, 99-491, 99-500, 99-591, 100-202, 100-436, and 101-166.

Part II - Data on Medicaid Financed Abortions

Following the implementation on February 14, 1978, of regulations which resulted from the Hyde Amendment, a specific reporting procedure was developed for reporting information on Medicaid financed abortions. Data are reported quarterly by the States on the numbers of abortions and the allowable abortion-related expenditures. Data on the number of reported abortions for FY's 1978 - 89 are given in Table 1 while expenditure amounts are given in Table 2.

Since February 14, 1978, 59,992 Medicaid financed abortions have been reported by forty-seven jurisdictions through September 30, 1989. Total Medicaid expenditures, including Federal and State shares, for abortions have been $16,570,656 during the period February 14, 1978 through September 30, 1989. Eight jurisdictions (American Samoa, Arizona, Hawaii, Michigan, New York, the Northern Mariana Islands, Puerto Rico and the Virgin Islands) have not claimed Federal funds for abortions. California has submitted claims for Federal Financial Participation (FFP) for abortions but has subsequently withdrawn these claims.

Of the 56 jurisdictions who reported for the period October 1, 1988 through September 30, 1989 (FY 1989), 13 jurisdictions claimed FFP under the Medicaid program for 48 abortions at a cost of $52,217 including both Federal and State shares. By comparison, 14 jurisdictions claimed FFP under the Medicaid program in FY 1988 for 94 abortions at a cost of $80,691 including both Federal and State shares. All abortion claims are subject to review by regional office staff. All claims found not to meet the applicable Federal criteria for FFP will be either withdrawn by the State or disallowed by HCFA.

The Health Care Financing Administration has not collected information on the number of abortions provided to Medicaid recipients where the State did not claim FFP, or on the number of Federally financed Medicaid abortions prior to the implementation of the regulations on the Federal financing of abortions on February 14, 1978.

The abortion data in the attached tables reflect the most current information available as of December 12, 1989. Because States submit revised abortion claim data, the data contained in this report may differ with information contained in reports previously issued.

TABLE 1
TOTAL NUMBER OF REPORTED MEDICAID ABORTIONS, BY STATE AND FISCAL YEAR
February 14, 1978 - September 30, 1989 1/

State	Total	FY 1978-1985 2/	FY 1986	FY 1987	FY 1988	FY 1989
Total	59,992	59,527	232	91	94	48
Alabama	599	560	12	7	18	2
Alaska	94	94	0	0	0	0
American Samoa 3/	0	0	0	0	0	0
Arizona 4/	0	0	0	0	0	0
Arkansas	325	321	3	1	0	0
California	0	0	0	0	0	0
Colorado	2,136	2,136	0	0	0	0
Connecticut	1,395	1,385	7	2	0	1
Delaware	328	318	6	2	2	0
District of Columbia	2,759	2,759	0	0	0	0
Florida	1,315	1,296	13	6	0	0
Georgia	860	839	7	6	6	2
Guam	5	5	0	0	0	0
Hawaii	0	0	0	0	0	0
Idaho	99	89	1	2	7	0
Illinois	3,217	3,203	2	2	5	5
Indiana	541	540	1	0	0	0
Iowa	335	308	6	5	9	7
Kansas	436	425	1	2	5	3
Kentucky	28	17	0	4	6	1
Louisiana	268	268	0	0	0	0
Maine	272	255	5	5	5	2
Maryland	4,260	4,260	0	0	0	0
Massachusetts	8,800	8,800	0	0	0	0
Michigan	0	0	0	0	0	0
Minnesota	1,593	1,574	3	3	9	4
Mississippi	13	13	0	0	0	0
Missouri	49	49	0	0	0	0
Montana	21	7	13	1	0	0
Nebraska	114	112	2	0	0	0
Nevada	122	122	0	0	0	0
New Hampshire	84	84	0	0	0	0
New Jersey	4,269	4,269	0	0	0	0
New Mexico	232	232	0	0	0	0
New York	0	0	0	0	0	0
North Carolina	1,438	1,407	12	5	4	10
North Dakota	6	6	0	0	0	0
N. Mariana 5/ Islands	0	0	0	0	0	0
Ohio	9,336	9,316	8	12	0	0
Oklahoma	356	356	0	0	0	0
Oregon	1,341	1,341	0	0	0	0
Pennsylvania	9,481	9,373	108	0	0	0
Puerto Rico	0	0	0	0	0	0
Rhode Island	5	5	0	0	0	0
South Carolina	511	481	6	8	8	8
South Dakota	1	1	0	0	0	0
Tennessee	388	365	6	10	5	2
Texas	73	73	0	0	0	0
Utah	280	280	0	0	0	0
Vermont	194	190	2	2	0	0
Virgin Islands	0	0	0	0	0	0
Virginia	124	107	6	6	5	0
Washington	350	350	0	0	0	0
West Virginia	3	3	0	0	0	0
Wisconsin	1,534	1,531	2	0	0	1
Wyoming	2	2	0	0	0	0

1/ Data for this report are taken from the 64.9 forms submitted by the Medicaid jurisdictions as part of their quarterly statement of expenditures. This report reflects the most current information available as of December 12, 1989. Because States submit revised abortion claim data, the data contained in this report may differ with information contained in reports previously issued.
2/ Data for FY 1978 are only for the period from February 14, 1978 through September 30, 1978.
3/ No Medicaid program in effect until FY 1982.
4/ No Medicaid program in effect until FY 1983.
5/ No Medicaid program in effect until FY 1979.

TABLE 2
TOTAL REPORTED EXPENDITURES FOR MEDICAID ABORTIONS, BY STATE AND FISCAL YEAR
February 14, 1978 - September 30, 1989 1/

State	Total	FY 1978-1985 2/	FY 1986	FY 1987	FY 1988	FY 1989
Total	$16,570,656	$ 16,171,143	$ 139,066	$ 127,539	$ 80,691	$ 52,217
Alabama	148,503	131,307	2,542	1,952	11,936	766
Alaska	36,331	36,331	0	0	0	0
American Samoa 3/	0	0	0	0	0	0
Arizona 4/	0	0	0	0	0	0
Arkansas	90,931	87,418	3,344	169	0	0
California	0	0	0	0	0	0
Colorado	496,239	496,239	0	0	0	0
Connecticut	521,940	516,216	4,916	588	0	220
Delaware	120,120	116,290	2,674	512	644	0
District of Columbia	371,040	371,040	0	0	0	0
Florida	329,746	302.513	8,515	18,718	0	0
Georgia	304,964	276,161	4,878	2,144	12,511	9,270
Guam	749	749	0	0	0	0
Hawaii	0	0	0	0	0	0
Idaho	28,965	24,328	481	502	3,654	0
Illinois	529,663	527,328	336	252	865	882
Indiana	132,371	132,091	280	0	0	0
Iowa	125,128	93,655	1,235	13,779	6,427	10,032
Kansas	145,800	140,623	912	470	2,766	1,029
Kentucky	30,563	9,425	0	6,547	14,407	184
Louisiana	48,900	48,900	0	0	0	0
Maine	108,670	99,894	2,582	2,517	2,743	934
Maryland	1,084,522	1,084,522	0	0	0	0
Massachusetts	1,117,351	1,117,351	0	0	0	0
Michigan	0	0	0	0	0	0
Minnesota	293,253	290,187	393	561	1,063	1,049
Mississippi	780	780	0	0	0	0
Missouri	3,217	3,217	0	0	0	0
Montana	5,713	2,857	2,638	218	0	0
Nebraska	27,749	27,504	245	0	0	0
Nevada	29,204	29,204	0	0	0	0
New Hampshire	12,319	12,319	0	0	0	0
New Jersey	884,071	884,071	0	0	0	0
New Mexico	43,360	43,360	0	0	0	0
New York	0	0	0	0	0	0
North Carolina	465,748	423,299	13,242	12,588	4,730	11,889
North Dakota	1,087	1,087	0	0	0	0
N. Mariana 5/ Islands	0	0	0	0	0	0
Ohio	5,506,544	5,451,477	20,712	34,355	0	0
Oklahoma	171,623	171,623	0	0	0	0
Oregon	157,373	157,373	0	0	0	0
Pennsylvania	2,371,222	2,314,246	56,976	0	0	0
Puerto Rico	0	0	0	0	0	0
Rhode Island	5,097	5,097	0	0	0	0
South Carolina	158,289	140,739	4,613	3,259	3,825	5,853
South Dakota	202	202	0	0	0	0
Tennessee	98,007	54,737	3,580	22,226	10,759	6,705
Texas	24,037	24,037	0	0	0	0
Utah	55,358	55,358	0	0	0	0
Vermont	48,104	42,732	2,880	2,492	0	0
Virgin Islands	0	0	0	0	0	0
Virginia	56,933	48,122	760	3,690	4,361	0
Washington	66,091	66,091	0	0	0	0
West Virginia	868	868	0	0	0	0
Wisconsin	310,173	306,437	332	0	0	3,404
Wyoming	1,738	1,738	0	0	0	0

1/ Data for this report are taken from the 64.9 forms submitted by the Medicaid jurisdictions as part of their quarterly statement of expenditures. This report reflects the most current information available as of December 12, 1989. Because States submit revised abortion claim data, the data contained in this report may differ with information contained in reports previously issued. The expenditures shown include both the Federal and State shares.
2/ Data for FY 1978 are only for the period from February 14, 1978 through September 30, 1978.
3/ No Medicaid program in effect until FY 1982.
4/ No Medicaid program in effect until FY 1983.
5/ No Medicaid program in effect until FY 1979.

Public Health Service

Acquired Immunodeficiency Syndrome

Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	[illegible]
National Institutes of Health:					
National Cancer Institute	$63,755,000	$89,944,000	$122,247,000	$150,304,000	$[illegible]
National Heart, Lung, and Blood Institute	17,244,000	24,885,000	38,088,000	42,056,000	[illegible]
National Institute of Dental Research	3,247,000	3,850,000	3,920,000	4,862,000	[illegible]
National Institute of Diabetes and Digestive and Kidney Diseases	495,000	3,330,000	3,557,000	5,320,000	[illegible]
National Institute of Neurological Disorders and Stroke	3,685,000	12,342,000	13,069,000	16,158,000	[illegible]
National Institute of Allergy and Infectious Diseases	145,760,000	223,298,000	311,277,000	393,958,000	[illegible]
National Institute of General Medical Sciences	5,420,000	7,724,000	10,830,000	14,614,000	[illegible]
National Institute of Child Health and Human Development	4,762,000	17,153,000	22,437,000	26,749,000	[illegible]
National Eye Institute	253,000	3,830,000	4,828,000	5,533,000	[illegible]
National Institute of Environmental Health Sciences	216,000	3,896,000	4,138,000	4,291,000	[illegible]
National Institute on Aging	184,000	361,000	443,000	854,000	[illegible]
National Institute of Arthritis and Musculoskeletal and Skin Diseases	100,000	561,000	673,000	1,238,000	[illegible]
National Institute on Deafness and Communication Disorders	---	---	---	---	[illegible]
Division of Research Resources	11,027,000	28,283,000	67,616,000	46,094,000	[illegible]
National Center for Nursing Research	---	612,000	703,000	987,000	[illegible]
John E. Fogarty International Center	---	4,505,000	4,619,000	4,894,000	[illegible]
National Library of Medicine	---	---	20,000	493,000	[illegible]
Office of the Director	4,759,000	5,636,000	12,865,000	10,551,000	[illegible]
Buildings and Facilities	---	370,000	5,772,000	14,765,000	[illegible]
Total, National Institutes of Health	260,907,000	430,570,000	627,101,000	743,532,000	[illegible]
Food and Drug Administration**	15,774,000	34,517,000	73,775,000	56,220,000	[illegible]
Centers for Disease Control	136,007,000	304,942,000	377,592,000	442,826,000	[illegible]
Alcohol, Drug Abuse, and Mental Health Administration	47,504,000	112,257,000	173,336,000	214,647,000	[illegible]
Health Resources and Services Administration*	11,900,000	36,956,000	59,945,000	112,503,000	[illegible]
Office of the Assistant Secretary for Health	30,363,000	4,046,000	13,270,000	7,676,000	[illegible]
Indian Health Service	---	---	800,000	---	[illegible]
Office of Health Care Policy and Research	---	---	---	8,474,000	[illegible]
Total, Public Health Service	502,455,000	923,288,000	1,325,819,000	1,585,878,000	[illegible]

* Includes $23,935,000 of two-year money in OPR and $872,000 of no-year money in BEF.
** Reflects Budget Authority

4

NATIONAL INSTITUTES OF HEALTH

Acquired Immunodeficiency Syndrome

The National Institutes of Health continues to expand basic studies and clinical research aimed at understanding, treating, and preventing human immunodeficiency virus (HIV) infection. Through basic research in virology, immunology, and molecular biology, scientists are rapidly accumulating new information about the immune mechanisms involving HIV infection, the structure of the virus, and the genetic variability of HIV. At the same time, clinical evaluation of vaccines, anti-retroviral drugs, and therapies for AIDS-related infections and cancers accelerates.

This research is being conducted through intramural studies, grants, collaborative agreements, and contracts. The National Institute of Allergy and Infectious Diseases (NIAID) leads the NIH AIDS research effort, with major contributions by the National Cancer Institute (NCI), the National Heart, Lung, and Blood Institute (NHLBI), the Division of Research Resources (DRR), and the National Institute of Child Health and Human Development (NICHD). The National Institute of Dental Research (NIDR), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Neurological Disorders and Stroke (NINDS), National Institute of General Medical Sciences (NIGMS), National Eye Institute (NEI), National Institute of Environmental Health Sciences (NIEHS), National Institute on Aging (NIA), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Center for Nursing Research (NCNR), Fogarty International Center (FIC), and the Office of the Director, NIH, are also conducting or supporting AIDS research. Moreover, many individuals infected with HIV have participated in studies of experimental AIDS therapies at the NIH Clinical Center (CC).

Many NIH activities are aimed at prevention and early diagnosis. The pursuit of these activities has become even more important since clinical trials during 1989 demonstrated the benefits of early treatment. More reliable methods of screening donated blood for human immunodeficiency virus (HIV) are being developed. In addition, better testing methods are needed for newborns because infants who have maternal antibody but are free of the virus can falsely test as seropositive. In addition, research to inactivate retroviruses in donated blood is focusing on filtration and chemical methods, because blood components such as the cryoprecipitate, which is a source of Factor VIII (used in the treatment of hemophilia), red cells, and platelet components, do not tolerate heat treatment.

New treatments, drug combinations, and the optimization of current therapies have been the focus of clinical trials in the NIH AIDS Clinical Trials Group. During 1989, important findings in several large trials demonstrated that early treatment with zidovudine (AZT) delays the onset of symptoms and progression of disease.

AZT is a potent inhibitor of HIV replication and is the only approved antiviral treatment for AIDS. Its usefulness is limited, however, by its side effects, particularly bone marrow depression. Basic laboratory research by NIH grantees suggests that the toxicity of AZT might be due to its effects on the replication of genetic material within the mitochondrion, one of the cell's organelles.

Another rapidly developing area concerns the consequences of HIV infection on the central nervous system. The neurological effects of AIDS, particularly dementia, greatly add to the personal suffering caused by AIDS. Recent studies are revealing some of the dynamics involved in AIDS dementia in adults. In children with AIDS, different types of abnormalities have been discovered, suggesting that pediatric AIDS dementia may be distinct from dementia in adult AIDS patients.

The development of various animal models for studying the structure and pathogenesis of HIV infection has been very important in the effort to understand and combat this complex disease. The development of the SCID-human mouse system has been particularly noteworthy. This mouse model, which has a human immune system, promises to be useful for studies of HIV pathogenesis and treatment. Additionally, the difficult challenge of developing an effective and safe vaccine against HIV infection hinges on research being carried out in non-human primates.

Research results are of little value if they are not easily accessible to scientists and clinicians, and at no time in history has this been more evident than with the AIDS epidemic. AIDS information services are needed to provide scientists, physicians, and other health professionals faster access to more complete information in AIDS research, diagnosis, treatment, control, and prevention. The National Library of Medicine has laid the foundation for such a data bank by initiating a bibliographic database called AIDSLINE, which contains some 22,000 references to scientific articles about AIDS. As part of the Public Health Service effort to make information on clinical trials and treatments available, NLM has added two new databases--AIDSTRIALS and AIDSDRUGS--to the library's network of online databases. In addition to the NLM databases, NIAID's AIDS Clinical Trials Information Service, a free telephone service at 1-800-TRIALS-A,

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provides the latest information on clinical trials to physicians, patients, and their families.

The face of HIV infection is changing from an acute illness to a chronic disease and from a disease confined largely to the homosexual population to an affliction of the inner city poor. The proportion of infection is rising among blacks, Hispanics, women and children. To reach these populations in the communities where they receive their medical care, in 1989 NIH launched an initiative called Community Programs for Clinical Research in AIDS. Eighteen contracts were awarded in fourteen cities where the impact of AIDS is severe, extending clinical trials of promising new therapies to physicians on the front lines of the epidemic who are involved in the day-to-day management of people infected with the virus. In addition, during 1989, NIH expanded the clinical trial network known as the AIDS Clinical Trials Group to include 15 pediatric units.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

NIAID conducts a comprehensive program to attack AIDS on several fronts. Basic research is focused on increasing the understanding of the structure and behavior of HIV and its pathogenic disease-producing activity, as well as immune responses to HIV infection. Epidemiologic studies in various population groups in the United States and around the world are amassing information on the natural history of the disease and its transmission. The development and testing of new drugs and strategies for treating HIV disease and its various manifestations are major priorities. To prevent the spread of HIV infection, the Institute is testing two AIDS vaccines in humans and supporting research to develop other candidate vaccines. Finally, important new programs have been launched to reach out to affected individuals and communities and increase their involvement in combatting the AIDS epidemic.

Preclinical AIDS Research Focuses on Disease Mechanisms

Basic research into the nature of the AIDS virus is the major focus of several laboratories of the NIAID intramural program. One group, under the direction of Dr. Anthony S. Fauci, NIAID Director, is studying the types of immune system cells that are infected with HIV and the ways in which the infection of these cells relates to HIV disease progression. Drs. H. Clifford Lane, Steven M. Schnittman, Fauci, and their colleagues are using the newly available research technique called polymerase chain reaction (PCR) to look for HIV-infected cells in AIDS patients. The highly sensitive PCR technique, by magnifying viral genetic material present in a cell, can detect HIV that is present in exquisitely small quantities.

Although AIDS patients typically display substantial defects in T cell number and function, clinicians have not been able to detect many HIV-infected T cells circulating in an infected person's blood. Using PCR, Dr. Schnittman reported that people with AIDS harbor 100 times more infected T cells than previously thought. HIV is present in at least 1 out of every 100 circulating T cells that carries a CD4 molecule. (The presence of the CD4 protein on a cell enables HIV to gain entry to the cell.) The research team further showed that 1 in every 1,000 CD4-positive (CD4+) T cells in AIDS patients is producing viral gene products capable of spreading HIV infection to other cells or producing other damage. Further, in contrast to T cells growing in culture, T cells in patients continue to have CD4 on their surfaces even after becoming infected with HIV. This research establishes the T4 cell as the main reservoir of HIV and demonstrates that these cells should be considered a target for drugs developed to arrest HIV infection.

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PCR is now used primarily as a research tool but, because it enables detection of HIV before viral antibodies appear in the blood, the procedure has potential for wide clinical application. In recognition of the potential importance of PCR, NIAID's Division of AIDS (DAIDS) initiated a PCR Standardization Project to evaluate the ability of clinical laboratories to use PCR. Nine laboratories are participating in this project, which is expected to define PCR procedures that will be sensitive, reliable, and reproducible in clinical laboratories.

The effects of other viral infections on HIV activation are being studied by NIAID contractor Dr. Kathleen Clouse of Georgetown University, Washington, D.C., and colleagues. In laboratory studies, they have shown that certain inactivated viruses, such as cytomegalovirus and Epstein-Barr virus, stimulate the cell to produce cytokines. These in turn augment HIV expression in HIV-infected promonocytes (a monocyte-like cell line). These results suggest that certain concomitant viral infections may be able to increase HIV production in HIV-infected persons.

Other studies are addressing the precise mechanisms of HIV infection and disease progression. This information is expected to provide insight into strategies to interfere with these mechanisms and thereby halt HIV-related disease progression in people who are already infected. Intramural scientist Dr. Scott Koenig and colleagues have developed a system that enables them to identify individual components of HIV that may provoke a protective immune response. Intramural scientist Dr. Malcolm Martin and colleagues are examining the functions of individual HIV genes and the role that HIV proteins play in interfering with cell function. NIAID's Dr. Ronald Willey identified a region of the gp120 envelope protein of HIV that is required for infectivity. Further study of the ninth gene of HIV, called vpu, discovered in 1988 by visiting associate Dr. Klaus Strebel, is providing new information about the gene's role in the HIV life cycle. Found to be present in AIDS patients, the protein coded for by this viral gene facilitates the release of virus particles from infected cells.

Dr. Bruce Chesebro and Ms. Kathryn Wehrly at NIAID's Rocky Mountain Laboratories in Hamilton, Montana, have developed a system that allows accurate counting of extremely low levels of HIV-producing cells. This assay is capable of detecting one virus-producing infected cell among 1 million uninfected cells and is effective for counting HIV-producing cells immediately after their isolation from AIDS patients. Dr. Chesebro's assay was effectively used recently by NIAID grantee Dr. Douglas Richman, University of California, San Diego, to demonstrate the emergence of AZT-resistant HIV.

NIAID intramural researchers are also involved in studies to develop promising future therapies for HIV infection. Drs. Edward Berger and Bernard Moss, with colleagues at NCI have produced a recombinant protein called CD4-Pseudomonas exotoxin A (CD4-PE40) that, in cell culture, attaches to and kills cells that are actively producing HIV. Previously, in the laboratory, recombinant soluble forms of CD4 (rsCD4), the receptor by which HIV enters cells, have shown promise for treatment of AIDS by preventing the virus from entering cells. The first clinical trials of rsCD4 alone began in August 1988. Dr. Berger and colleagues are hopeful that the hybrid toxin CD4-PE40 will have a therapeutic effect in AIDS patients by eliminating HIV-infected cells.

Drug Development Bridges Basic Research and Clinical Treatment

The development of new safe and effective therapies for treating HIV and its associated opportunistic infections is one of NIAID's primary research goals. Such therapies must be first designed or discovered and then tested, first in the laboratory in test tubes, then in animals, and finally in human subjects.

To foster the development of new drugs, NIAID established a coordinated and comprehensive program, the National Cooperative Drug Discovery Groups for the Treatment of AIDS (NCDDG-AIDS). These 28 groups are composed of teams of experts from biotechnology companies, pharmaceutical firms, universities, medical centers, and Federal agencies. The purpose of the NCDDGs is to increase the likelihood of identifying or designing effective drug therapies for AIDS by bridging the gaps between the development of ideas and leads from basic research, drug discovery, and experimental testing and application.

Scientists under the leadership of Dr. John Zaia of the NCDDG at the City of Hope National Medical Center, Duarte, California, are working on synthetic ribozymes as a potential anti-HIV therapy. Ribozymes are enzymes that cleave and destroy RNA enzymes in a specific manner. Dr. Zaia and colleagues are constructing synthetic ribozymes consisting of HIV RNA bound to a suitably designed drug that will bind to and attack the HIV RNA, thereby rendering it nonfunctional. Preliminary findings of this novel approach to therapy indicate that ribozymes are effective in reducing HIV replication in cultured cells.

Two NCDDG groups have described inhibitors of HIV protease, an enzyme required in later stages of HIV replication when new virus particles are formed and released. Because HIV protease is critical in the production of virus by latently infected cells, inhibitors

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of protease function are expected to inhibit HIV production from these cells.

Dr. Steven Petteway and coinvestigators at Smith Kline and French Laboratories, a component of the NCDDG led by Dr. William Haseltine of the Dana Farber Cancer Institute in Boston, have been studying HIV protease as a target for selective antiviral agents. Recently, the group reported that certain synthetic peptides preferentially inhibit HIV protease and, more important, inhibited HIV replication in cultured cells. Studies to further evaluate the activity and toxicity of these peptides are in progress.

Another NCDDG team led by Dr. Garland Marshall at Washington University, St. Louis, Missouri, also identified certain synthetic peptides that inhibit HIV protease and viral replication in cultured cells. This group is collaborating with investigators at NCI to determine the crystalline structure of an HIV protease-inhibitor complex.

Because of the early success of the NCDDG-AIDS in bringing together investigators from diverse fields in productive collaborations, a similar program is being launched by NIAID to find new or improved therapies to treat the opportunistic infections associated with AIDS.

NIAID contractor Dr. Peter Walzer of the University of Cincinnati in Ohio has developed a synthetic growth medium that supports the growth of Pneumocystis carinii in culture in the absence of mammalian cells. P. carinii pneumonia (PCP) is the most common life-threatening opportunistic infection in HIV-infected patients. Previously belived to be a protozoa, this organism has recently been shown to contain a genetic makeup more closely aligned with fungi. The new growth medium, based on nutrient requirements for fungi, rather than those for protozoa, facilitates the study of P. carinii metabolism as well as the design of more effective and specific antimicrobial therapies. The new growth system also constitutes a practical and inexpensive drug evaluation system, making possible the screening of more candidate antimicrobial drugs than current screening methods allow.

Centers for AIDS Research -- New Grants Awarded

NIAID awarded four new 5-year grants within the past year to Duke University, Durham, North Carolina; the Johns Hopkins University, Baltimore, Maryland; New York University, New York City; and the Dana-Farber Cancer Institute, Boston, Massachusetts, to establish Centers for AIDS Research (CFAR). This brings the total number of CFARs to 11. The CFAR program was established to promote the development of new scientific knowledge about AIDS, with the ultimate goal of improving its diagnosis, treatment, and

prevention. CFAR grants are designed for investigators with established reputations for excellence in AIDS research who are already receiving funds for AIDS-related research from NIAID and other NIH institutes. The awards provide core support for consolidating and focusing the AIDS research activities at their universities.

Current scientific opinion recognizes that the epidemic of HIV infection requires a multidisciplinary approach involving a wide spectrum of basic, preclinical, clinical, and applied research. The directors of the CFARs are expected to provide strong leadership in facilitating creative, interactive AIDS research activities among a variety of laboratory and clinical investigators. Laboratory and clinical equipment or services that will be shared by a number of investigators engaged in AIDS research may be funded by the center grants. The CFAR program also makes funds available for upgrading laboratories and providing proper containment facilities for working with HIV and related retroviruses. NIAID has asked that special efforts be made to attract and support qualified minority and women scientists.

Animal Models Developed for AIDS

An important area of preclinical AIDS research is the development of animal models in which the virus and its effects can be studied. Information about how HIV induces disease in infected individuals and ultimately destroys the immune system cannot be learned from tissue culture systems currently available. Because harmful viral effects in a living person may be closely tied to complex, ongoing processes--such as metabolism or an active immune response--that cannot be duplicated by computer models or in cell cultures, development of appropriate animal models is critical. A variety of animals that are subject to AIDS-like viral diseases are also being used to test the efficacy and toxicity of new AIDS therapies and vaccines and to define the most effective combinations of drugs against HIV and its associated opportunistic infections.

One promising mouse model was developed by NIAID intramural scientists Drs. Martin and John M. Leonard and colleagues. The research team produced mice with complete copies of HIV genetic material in every cell of their bodies. Because they contain genetic material from another organism--HIV--in addition to their own, the mice are called transgenic. The researchers found that some of these mice spontaneously developed disease with many of the symptoms of AIDS. These unique mice were accidentally killed in a power failure, and the investigators are producing a new mouse colony. In collaboration with NIDR intramural scientists, Dr. Martin and colleagues have constructed transgenic mice containing the individual HIV genes env and nef and are

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evaluating them for disease induction. These animals will be very useful in evaluating drugs that delay or abrogate disease.

Scientists supported by NIAID are continuing to make progress in work with two mouse models developed last year. Mice born with a genetic defect called severe combined immune deficiency syndrome (SCID) lack a functional immune system. To create a model for human disease, researchers are reconstituting the immune system of these SCID mice with transplants of human materials. Because they lack their own immune cells, these animals do not reject transplanted human cells and tissue. The SCID mice offer a unique opportunity to study the effects of therapies against HIV or other infections directly on human cells in vivo (in a living organism).

Dr. Michael McCune, an NIAID contractor working with SyStemix, Palo Alto, California, is continuing work with an experimental SCID mouse model originally funded by an NIAID grant to Dr. McCune and colleagues at Stanford University. The immunocompromised mice were implanted with pieces of human fetal tissue, obtained under strict human use guidelines, which resulted in the production of human mini-organs that generate blood-forming and immune cells. Since the model was first described in 1988, the investigators demonstrated that the human immune cells in the mice can be infected with HIV. Current studies are examining the effectiveness of antiretroviral agents such as AZT to prevent disease and to treat.

In another approach, Dr. Donald Mosier and colleagues at the Medical Biology Institute, La Jolla, California, have reconstituted the immune systems of SCID mice with human peripheral blood lymphocytes. These mice produce human immunoglobulins and, when injected with substances that normally produce an immune response, have shown human antibody responses. This model has also been infected with HIV; one-quarter of the infected mice develop a wasting syndrome, a prominent feature of AIDS in humans. In addition, SCID mice develop PCP. The animals should be useful in studying the disease-producing effects of HIV and for evaluating potential therapies against both HIV and PCP.

NIAID-sponsored research has led to the development of animal models for studying how murine (mouse) retroviruses are transmitted from mother to offspring. Potentially, transmission of HIV from mother to infant may occur across the placenta, during the birth process, or through breast milk. NIAID-supported contractors Dr. Ruth Ruprecht at Dana-Farber Cancer Institute and Dr. John Bilello at the Veterans Administration Medical Center, Baltimore, have found that murine retroviruses can be transmitted through milk from infected lactating mice to their offspring.

Studies of placental transfer in mice showed that the sooner AZT is administered after exposure to the retrovirus, the better the chances of preventing disease.

A potentially important animal model for the study of HIV infection and AIDS is a rabbit model developed by Dr. Thomas J. Kindt, Dr. Henrietta Kulaga, and colleagues. The researchers have infected rabbits with HIV by injecting them with HIV-infected human T cells. The research team has identified parameters of infection necessary for standardized use of the rabbits in AIDS vaccine and drug development. A patent has been filed covering these procedures. Dr. Kindt and colleagues are also using their rabbit model to study where HIV goes in the body, details of the infectious process, whether the rabbit immune system is compromised, and how this can be measured.

NIAID contractors at Georgetown University Drs. Philip Johnson, Vanessa Hirsch, and Robert Olmsted along with NIAID intramural scientist Dr. Robert Purcell and colleagues are developing cat and monkey models of infection with HIV-related viruses. The researchers are studying the pathogenic effects of the feline immunodeficiency virus (FIV), first isolated in 1986. In April 1989, Dr. Johnson and his colleagues were the first to publish an article on the molecular cloning of FIV--that is, the procedure by which researchers determine the precise message in FIV's genetic information.

Dr. Johnson and colleagues are also studying the simian immunodeficiency virus (SIV) in macaque monkeys. Like HIV, FIV and SIV are members of the lentivirus (slow virus) family. The researchers are interested in how genetic variations between individual FIV and SIV isolates affects disease progression in their hosts. This information has important implications for development of HIV therapies and vaccines.

Dr. Louis Martin at the Delta Primate Center, Tulane University, New Orleans, Louisiana, is also investigating SIV infection in macaque monkeys. Under contract to NIAID, Dr. Martin and colleagues have identified a specific kind of lymphocyte, a CD4 positive, helper-inducer T cell, similar to the human cell, that is selectively depleted in SIV disease. Selective depletion of this cell type is predictive of the severity and course of SIV disease. This finding may be applicable to humans with HIV infection and used to predict whether individuals will succumb rapidly or survive longer. Such information may be of particular value in decisions about therapy.

The major limiting factor in these studies is the lack of sufficient numbers of macaque monkeys. Dr. Susan Ellenberg of NIAID and Dr. Dale Spriggs, formerly of DAIDS, have

developed statistical approaches to designing more efficient strategies for conducting drug and vaccine trials in SIV animal models, which in turn may improve the chances of quickly identifying promising agents for clinical trials.

Georgetown University investigators Drs. Hirsch, Johnson, and Olmsted, along with Dr. Michael Murphey-Corb of the Delta Regional Primate Center, and NIAID's Dr. Purcell have new evidence that a virus isolated from a species of West African monkey may have successfully infected humans 20 to 40 years ago and subsequently evolved into the second known AIDS virus, HIV-2.

Epidemiology Provides Insights into Disease Patterns and Effects

Epidemiologic studies provide the information that enables investigators to characterize the natural history of AIDS, identify the mechanisms of disease transmission, and determine the nature and extent of infection in high-risk populations.

The NIAID-supported Multicenter AIDS Cohort Study (MACS), begun in 1984, is the largest and most productive prospective epidemiologic study of AIDS. Currently, nearly 5,000 homosexual and bisexual men participate in the study, which is conducted at four sites in the United States: the Johns Hopkins University; University of California, Los Angeles, School of Public Health; Northwestern University Chicago, Illinois; and the University of Pittsburgh in Pensylvania. The MACS yields information on the principal modes of transmission of HIV, factors that increase or decrease the likelihood of infection, factors that might promote or protect against the expression of HIV, and the clinical manifestations of the disease. An integral part of this study is the collection of biological specimens (urine, blood, semen, etc.), which are maintained for future study.

The MACS has provided much valuable information about the onset of HIV disease and factors associated with rapid or slow progression of disease. Several important findings from the study were reported jointly by MACS research teams during the past year.

Investigators at the four MACS sites conducting a neuropsychological study with 1,550 men reported finding no mental impairment in asymptomatic men infected with HIV. The men had undergone neuropsychological testing every 6 months for 3 years. This study confirmed earlier reports that the frequency of neurologic abnormalities among asymptomatic HIV-infected homosexual men is low and not different from that seen in uninfected homosexual men. This is the first study to document continuing normal cognitive function over a long period with a large group of infected

persons. While many AIDS patients suffer dementia and neurologic illness as they approach later stages of the disease, this study indicates that asymptomatic people infected with HIV are capable of holding jobs that demand good cognitive performance and responsibility for public safety.

MACS investigators Dr. Justin C. McArthur and colleagues at the Johns Hopkins University studied the cerebrospinal fluid (CSF) of 25 men in the MACS cohort. The investigators observed that changes in the CSF profile correlated with changes in peripheral blood CD4 lymphocytes, and concluded that declining immune status was associated with CSF abnormalities, possibly reflecting increased HIV activation within the central nervous system. Longitudinal studies in a larger group, however, are necessary to determine whether CSF changes are truly predictive of declining immune status.

The same research team also examined the effects of AZT on neurological status and neuropsychological performance of men enrolled in the MACS. Preliminary observations indicate that neuropsychological performance can stabilize or improve after administration of AZT. The study team reported MACS data showing that prior syphilis infection is not associated with a higher rate of CSF abnormalities, thus suggesting that a previous syphilis infection does not lead to increased HIV-1 activation within the central nervous system. NIAID grantees Drs. Margaret Ragni and Laurence Kingsley of the University of Pittsburgh studied 84 HIV-positive persons with hemophilia who were cared for at the Hemophilia Center of Western Pennsylvania. The study findings point to age-related differences in the onset of AIDS and in the lifespan of patients once they develop AIDS. The older these hemophiliac patients were when they became infected with HIV, the sooner they showed signs of illness, and the shorter their survival. The research team found that, after a 6-year period of infection, 49 percent of patients over age 30 had developed AIDS, compared to 24 percent of the 18- to 30-year-old group had developed AIDS, and only 5 percent of patients under age 18. The study suggests that age of patients is important in progression to AIDS and needs to be considered when designing antiviral therapies for patients.

NIAID grantee Dr. Jay A. Levy and colleagues at the University of California, San Francisco, studied a group of children born to mothers infected with HIV. Because these babies carry maternal antibodies to HIV, while most of those who are truly infected with HIV are asymptomatic during the first 3 months of life, diagnosis during this period is difficult. Yet early diagnosis is critical for the early initiation of treatment and planning of future care for the infant as well as for the emotional well-being of the parents. The research team reported that as many as 60

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percent of infants of infected mothers may be infected by HIV. The investigators found that viral culture techniques to detect HIV were valuable for early diagnosis of maternally transmitted HIV infection.

In 1989, NIAID awarded three 5-year contracts for a collaborative prospective study of the transmission and natural history of HIV infection among heterosexuals. The 2,000 men and women enrolled must not be IV drug users but should be at high risk for HIV infection. Two study centers, one in Newark, New Jersey, and one in Brooklyn, New York, were funded, as was a data coordinating center in Ann Arbor, Michigan. The study sites were chosen in part because of their location in inner-city areas populated by large numbers of HIV-infected IV drug users, a potential reservoir of infectivity for heterosexuals. The overall goals of the study are to determine the natural history of HIV infection in heterosexual women and men who have no history of IV drug use, to identify the sexual and other behaviors associated with the transmission of HIV in such a population, and to determine the biological and environmental cofactors associated with the acquisition or severity of the expression of HIV infection in such a population. Educational intervention strategies will also be assessed.

Clinical Trials Expanded

NIAID conducts and supports intramural and extramural research aimed at developing safe and effective therapies for HIV infection and associated opportunistic infections and cancers. By expanding and modifying its AIDS Clinical Trials Program, NIAID has achieved greater collaboration among investigators in the nationwide treatment evaluation network and greatly accelerated development of new high-priority clinical trials of promising therapies.

Through cooperative agreements, NIAID funds 47 AIDS Clinical Trials Units (ACTUs), including 15 pediatric units, which conduct both large multicenter trials and some smaller single-institution studies. The AIDS Clinical Trials Group (ACTG) is composed of all of the ACTUs, the Clinical Trials Coordinating Center (which collects and analyzes data from the studies), and the NIAID Division of AIDS. The ACTG examines the efficacy of new therapies, develops new drugs from preclinical study to final approval by the Food and Drug Administration (FDA), and ensures the effective transfer of therapies from the research setting to physicians providing routine patient care.

As of October 1989, more than 8,200 persons had participated in ACTG studies. More than two dozen drugs, including antiviral agents, biologic response modifiers, and drugs for opportunistic infections, were under study alone

or in combination. Studies cover the full range of HIV infection and associated clinical problems, including AIDS-related malignancies and HIV disease in children.

Studies continue to demonstrate the effectiveness of AZT in extending the lives of persons with AIDS. AZT is the only anti-retroviral drug approved for the treatment of patients with AIDS and AIDS-related complex (ARC).

AZT is one of a number of nucleoside analogues that are being studied for their anti-HIV effects. To HIV, these analogues look like nucleosides, the building blocks of an organism's genetic material. The virus is fooled into employing these fake molecules during viral replication, thereby disrupting the production of new virus particles.

In two large placebo-controlled clinical trials conducted by the ACTG, AZT was found to significantly slow the progression of HIV disease in persons with early ARC and in HIV-infected asymptomatic persons with CD4+ T-cell counts below 500. Because AZT was so clearly effective, NIAID halted both studies on the recommendation of a Data and Safety Monitoring Board and instead offered AZT to all study participants. The evaluation of AZT in asymptomatic HIV-infected persons will continue for those whose CD4+ T-cell counts remain above 500, as the short-term risk of developing AIDS symptoms appears to be negligible in this group.

The study participants who received AZT experienced few serious side effects. The study of patients with ARC was chaired by NIAID grantee Dr. Margaret Fischl, University of Miami School of Medicine, and the study of asymptomatic HIV-infected persons was chaired by NIAID grantee Dr. Paul Volberding, University of California at San Francisco and San Francisco General Hospital. NIAID will convene a state-of-the-art panel to develop recommendations for using AZT to treat persons with early HIV disease.

In one of the multicenter ACTG studies involving AZT, Dr. Fischl compared the long-term safety, tolerance, and efficacy two dose regimens of oral AZT in persons with AIDS who had recovered from one episode of PCP. Preliminary analysis indicates that survival rates were approximately equivalent for patients in the high- and low-dose groups. Blood toxicities, especially decreases in numbers of neutrophils (a type of white blood cell), were less common in the group receiving the lower doses. The investigators are evaluating the time it took for the study patients to develop opportunistic infections and the degree of improvement in neurologic disease or other serious consequences of HIV infection.

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A new NIAID-sponsored clinical trial, to be conducted at the University of Miami and the UCLA School of Medicine in Los Angeles, will evaluate the safety and pharmacokinetics (drug levels and absorption) of intravenous and oral AZT administered to HIV-infected asymptomatic women during the last trimester of pregnancy and at delivery. This information is needed before studies can evaluate AZT's effectiveness in reducing the rate of HIV transmission from mother to baby. Children with HIV usually develop disease more quickly than adults and, of those diagnosed before their first birthday, half die within 6 months of diagnosis.

Infants born to HIV-infected mothers were studied in a Phase I ACTG trial, chaired by Dr. John Modlin at the Johns Hopkins University. Asymptomatic babies younger than 3 months old were treated with oral doses of AZT. While the trial is not complete, preliminary results indicate that AZT was well tolerated by the infants. The dose of AZT given to infants resulted in concentrations of drug in the blood comparable to those obtained in adults receiving therapeutic doses.

Based on ACTG studies using AZT in children with HIV disease and studies sponsored by the drug manufacturer, Burroughs Wellcome Co., Research Triangle Park, North Carolina, the FDA granted Treatment IND status (a category that allows patients with serious or life-threatening conditions to receive experimental drugs before the completion of efficacy trials) for the use of AZT in children under 13 who have AIDS or have symptoms of advanced infection with HIV. The Treatment IND is sponsored by Burroughs Wellcome, with medical and technical assistance provided by NIAID.

The efficacy of AZT in alleviating mild to moderate AIDS dementia complex (ADC) in HIV-infected patients is being evaluated in an ACTG multicenter trial headed by Dr. Richard Price, formerly of Memorial Sloan-Kettering Cancer Center, New York, and now at the University of Minnesota ACTU. Preliminary results suggest that AZT improves neuropsychological performance in ADC patients. Final analysis is not yet complete.

Although AZT has become the standard therapy for persons with AIDS and AIDS-related complex, the drug reduces both red and white blood cells and thus its use can lead to anemia and susceptibility to infections. NIAID is conducting and supporting studies of AZT that are directed at improving its activity and reducing its toxicity. Drs. David Kornhauser and Paul Lietman and colleagues at the Johns Hopkins University used AZT in combination with probenecid (a drug used to treat gout) to treat eight men diagnosed with AIDS or ARC. They found that the addition of probenecid nearly doubled the blood levels of AZT compared

to persons taking AZT alone. Probenecid was developed in the 1940's to slow down the kidney's elimination of penicillin from the body and thus prolong its activity.

While numerous studies were documenting the value of AZT, it was also reported that AZT-resistant strains of HIV had been isolated from patients with AIDS or advanced ARC who had taken the drug for more than 6 months. Longer durations of treatment were associated with progressively greater resistance of the viral isolates. Thus far, however, no correlation has been found between in vitro resistance and the clinical condition of the patients. This preliminary finding was reported by NIAID grantee Dr. Douglas Richman, University of California, San Diego, and colleagues at Wellcome Research Laboratories.

In response to the urgent need to identify alternative therapies to AZT, FDA and NIAID developed a comprehensive plan for the clinical evaluation and expanded availability of dideoxyinosine (ddI), a chemical relative of AZT. This promising antiviral agent has shown activity against HIV in laboratory studies and in initial human studies carried out by NCI, although some persons have experienced potentially serious effects. Under this plan, clinical trials designed to determine the safety and effectiveness of ddI are being conducted by the ACTG in collaboration with Bristol-Myers Company, New York, the drug manufacturer. Three Phase II clinical trials will enroll approximately 2,600 persons with AIDS or ARC.

Simultaneously, FDA granted Bristol-Myers permission to distribute ddI through a Treatment IND for patients with AIDS or advanced ARC who cannot take AZT because of serious drug toxicity, and similar permission to distribute ddI under an open safety protocol for AIDS patients whose disease has substantially progressed despite AZT therapy and who have no other treatment options. NIAID provided technical assistance to the company in preparing the Treatment IND protocol.

Dideoxycytidine (ddC) is another promising nucleoside analogue being studied by the ACTG. ACTG investigator Dr. Thomas Merigan at Stanford University has shown that ddC, when given in low doses, only occasionally caused the painful nerve problems in the feet and legs associated with high-dose ddC therapy. Moreover, when ddC is given in very low doses, it suppresses HIV replication in people with AIDS and is even more effective in people with ARC. Because side effects of low but effective doses are minimal, researchers have expanded clinical testing of the drug. Studies comparing ddC used alone or alternating with AZT are under way in the ACTG. Use of ddC appears promising in persons who cannot tolerate AZT and, because the side effects of AZT and ddC treatment appear not to overlap, it may be possible

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to treat patients with alternating regimens of the two drugs.

Two antiretroviral drugs developed by NCDDG investigators entered clinical trials in 1989. The first, CS-87, or azidouridine (AzdU), is a nucleoside analogue first synthesized by Dr. Tai-Shun Lin of Yale University, New Haven, Connecticut. AzdU's anti-HIV activity was discovered by Dr. Raymond Schinazi at Emory University/Veterans Administration, Atlanta, Georgia, principal investigator of an NCDDG team, and Dr. Chung K. Chu at the University of Georgia in Athens. AzdU is licensed by Triton Biosciences, Inc., Alameda, California. A Phase I study being is conducted at NIH's Clinical Center by NIAID intramural scientist Dr. Lane and Dr. Henry Masur, CC, to help determine the maximal tolerated dose of AzdU and to provide data on the drug's potential antiviral and immunomodulating effects. In vitro and animal studies show that AzdU may be less toxic than AZT.

The second NCDDG-developed compound, d4T, another nucleoside analogue, also compares favorably to AZT in antiretroviral activity and may be less toxic to human bone marrow cells. The drug was developed by Drs. Lin and William Prusoff (Yale University and a member of Dr. Schinazi's NCDDG team) and is licensed by Bristol-Myers. Like AZT, d4T inhibits HIV reverse transcriptase, an enzyme necessary for the virus to replicate, but it does not have the metabolic byproducts that have been shown to cause AZT's toxic side effects. Phase I clinical studies of d4T will compare the safety, pharmacokinetics, and preliminary efficacy of up to nine different dosage levels of oral d4T. A total of 45 people with AIDS or ARC will be enrolled at New York City's Mount Sinai and Cornell University ACTUs.

Several other promising anti-HIV drug candidates are being studied by Drs. Lane and Fauci in NIAID's intramural program. Alpha interferon, a powerful naturally occurring protein produced by the immune system, has been found by these and other investigators to have antitumor, immunomodulatory, and antiviral activities. FDA approval of alpha interferon for the treatment of AIDS-associated Kaposi's sarcoma in late 1988 was based largely on studies conducted by Drs. Lane and Fauci.

These investigators have reported that alpha interferon also appears to slow HIV production and reduce the risk of developing AIDS-related opportunistic infections in asymptomatic HIV-infected persons. They reported that alpha interferon decreased the rate of decline of CD4+ T-cells. Of the patients receiving the drug in their study, 64 percent developed persistently negative HIV cultures and, even after completion of therapy, none developed an AIDS-defining opportunistic infection. Adverse reactions to the

drug, which include flu-like symptoms and, less commonly, more severe side effects, often necessitate reductions in dose.

Another study by Drs. Lane and Fauci and colleagues confirmed that alpha interferon can be combined safely with AZT to treat AIDS-related Kaposi's sarcoma and suggested that the combination might be more effective than either drug alone at killing HIV. To establish whether the combination is more effective or less toxic than either drug alone, Dr. Lane and his coworkers are conducting a randomized clinical trial at the NIH Clinical Center.

In a Phase I trial of alpha interferon and AZT in AIDS-associated Kaposi's sarcoma, NIAID grantee Dr. Susan Krown of Memorial Sloan-Kettering Cancer Center confirmed that the two drugs could be combined safely and, in some patients, could induce a high tumor response rate and suppression of p24 (a measure of viral activity). In another study led by Dr. Krown, it was found that the response of Kaposi's sarcoma to alpha interferon treatment could be predicted by measurements of interferon, as well as blood levels of two substances known as beta-2 microglobulin and neopterin.

NIAID and Biogen, Inc., a biotechnology company located in Cambridge, Massachusetts, are sponsoring clinical tests of recombinant soluble CD4 (rsCD4) in patients infected with HIV. The studies, being conducted by ACTG investigators Drs. Robert Schooley at Massachusetts General Hospital and David Ho, Cedars-Sinai Medical Center, Los Angeles, are based on the knowledge that HIV gains entry into human cells by attachment of the virus envelope protein to the CD4 receptor, a protein on the surface of specific immune cells, especially T4 cells. The rsCD4 acts as a chemical decoy, binding with HIV in the body and blocking its capacity to cause infection. In laboratory experiments, rsCD4 was shown to block infection of T4 cells and cell to cell transmission of HIV. A Phase I dose escalation study designed to determine the safety of the drug, conducted in patients with AIDS and ARC, indicates that rsCD4 was well tolerated for periods of up to 1 month.

Preliminary results of a study which compared how readily the body absorbs single doses of oral or intravenous dextran sulfate suggest that the drug is minimally absorbed when taken by mouth. The scientists who conducted this bioavailablity study, NIAID grantee Dr. Paul Lietman and his collegues at the Johns Hopkins University Hospital and investigators at FDA, think it is very unlikely that the drug would be better absorbed if given at higher doses or over a longer period of time. An ongoing NIAID-sponsored clinical trial is evaluating dextran sulfate's promise as an AIDS drug.

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Patients are being enrolled in NIAID-sponsored ACTUs at the University of California at San Diego, Massachusetts General Hospital, and the University of Miami in a Phase I study of the antiviral drug N-butyl DNJ (NbuDNJ, also known as SC-48334). The investigators will test the safety and tolerability of a range of doses of NbuDNJ in patients with AIDS or advanced ARC. NbuDNJ is the first of a new class of compounds, called glucosidase inhibitors, to enter clinical trials. While AZT blocks an early step in viral replication, NbuDNJ interferes in the late stages of viral growth when the viral attachment apparatus, the envelope glycoprotein (gp120), is being made.

In light of the fact that PCP is the leading cause of morbidity and mortality in adult AIDS patients, NIAID convened a Public Health Service (PHS) task force to address PCP prophylaxis. The task force considered findings from the NIAID-sponsored MACS and from a comparative dose trial of aerosolized pentamidine (AP) conducted by the San Francisco Community Consortium, a group of independent physicians. Based on those same data, FDA granted LyphoMed, Inc., Rosemont, Illinois, a Treatment IND for AP. NIAID provided technical assistance and advice in the design and administration of the Consortium trial, which LyphoMed partially underwrote. Through a Treatment IND, AP was provided to HIV-infected individuals at high risk of developing PCP. As recommended by the PHS task force, AP was subsequently approved for use in HIV-infected individuals who have had at least one PCP episode or who have T4 cell counts lower than 200. The PHS then incorporated these recommendations into new guidelines for PCP prophylaxis.

A number of other agents are being evaluated for their potential value in treating opportunistic infections associated with AIDS. Dr. Judith Feinberg of the NIAID Division of AIDS reported that the experimental drug trimetrexate is effective and well tolerated by AIDS patients with PCP whose therapeutic options have been exhausted.

Clinical trials of the experimental antiviral drug foscarnet are being conducted, enrolling AIDS patients with cytomegalovirus (CMV) retinitis who cannot be treated with ganciclovir. Foscarnet does not affect the white blood cell count, and it has shown activity against HIV itself. Studies of foscarnet are being conducted by a group of intramural investigators at NIAID, NEI, and the Critical Care Department, CC, at NIH as well as at several ACTUs. Co-principal investigators of the ACTG studies are Dr. Mark Jacobson of the University of California, San Francisco, and Dr. Clyde Crumpacker of Harvard Medical School.

As the number of potential therapies for HIV infection increases, it will become more and more difficult to perform the randomized clinical trials required to evaluate promising therapies in a timely manner. Because the clinical progression of HIV infection can often be predicted by the level of certain biochemical, immunologic, and virologic markers, considerable interest has developed in substituting these "surrogate" markers for clinical endpoints, such as death or serious infection, as a way to shorten the time needed to evaluate new therapies. Dr. Ellenberg and her colleagues in NIAID's Division of AIDS have developed a statistical model of the chronological progression of the disease, including the occurrence of certain marker-based events (e.g., a drop in CD4+ cells below a certain level). Using computer simulation techniques, the investigators can quantitate the reliability of marker-based endpoints compared with clinical endpoints.

Community Programs for Clinical Research on AIDS Funded

During the past year, NIAID established the Community Programs for Clinical Research on AIDS (CPCRA), headed by Dr. Lawrence Deyton of NIAID's DAIDS. In the fall of 1989, NIAID funded 18 pilot programs in 14 cities to test different models for conducting clinical research in community settings. The new initiative expands NIAID's clinical investigations by including primary care physicians who are not affiliated with AIDS research efforts currently supported by NIAID. The program places importance on increasing the patient population base for AIDS clinical research by including more HIV-infected black and Hispanic persons and IV drug users, and more women at risk of HIV infection, groups in which the incidence of HIV infection is increasing rapidly. The research settings and methods are expected to differ from those of traditional clinical research. The community programs operate separately from, but work closely with, the existing ACTUs and will not replicate their structure, functions, or research. A request for proposals has been issued to establish a CPCRA data coordinating center.

Parallel Track Strategy Developed

In June 1989 Dr. Fauci proposed a "parallel track" system of clinical trials that would permit access to selected promising AIDS drugs while they are still being evaluated and before they are approved for marketing. The system would be intended for persons who are unable to participate in conventional clinical trials and cannot tolerate available therapies. The parallel track would enable them to obtain, through private physicians or through community-based clinical research programs, experimental drugs that have been shown to be safe and possibly efficacious in a Phase I or pilot study. The parallel track would be

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conducted simultaneously with Phase II trials that collect data on safety and efficacy in large numbers of patients. Adverse reaction data would be gathered on all persons participating in the parallel track. Decisions about patient eligibility would be determined by qualified physicians on a case-by-case basis.

A task force was formed to advise Public Health Service officials about guidelines and implementation of a parallel track system. The members of the task force include Dr. Fauci, Acting Director of NIH Dr. William Raub, two representatives from FDA, three representatives from AIDS advocacy groups, a clinical researcher, a community physician, and a representative from the drug abuse treatment community.

Vaccine Development and Testing Advances

The identification of vaccine candidates and their preclinical evaluation are being accomplished by 11 National Cooperative Vaccine Development Groups (NCVDGs), representing collaborations of researchers from industry, academia, and Government. Clinical trials of candidate vaccines are carried out by 6 NIAID Vaccine Evaluation Units (VEUs).

AIDS vaccines using either an inactivated whole or live attenuated virus carry some potential risks. The use of inactivated whole virus could introduce viral genetic material into cells of the body, while live attenuated virus could mutate and become pathogenic (disease-causing). Consequently, other types of vaccines are being considered. However, these other products have potentially lower immunogenicity (ability to provoke an immune response) and would have to be accompanied by adjuvants, or boosters, whose function is to induce a stronger immune response. To stimulate research on novel vaccine-adjuvant combinations, NIAID established the AIDS Cooperative Adjuvant Group (ACAG). Originally compised of 10 collaborating groups of researchers, in 1989 the ACAG was expanded by NIAID to 16 groups.

A new AIDS Vaccine Selection Committee was established to help decide which of the many potential AIDS vaccines now being tested in laboratories are promising enough to be tested in humans. With more than a dozen candidate vaccines in various stages of laboratory testing and several more on the drawing boards, AIDS vaccine development has accelerated to the point where uniform guidelines are needed to evaluate the products.

Current studies are evaluating each of the HIV virus proteins as possible vaccine candidates. The first vaccine approved in the United States for testing in Phase I

clinical trials is based on gp160, the precursor molecule of the two proteins that form the AIDS virus coat. Studies have shown that following infection with HIV, the immune system recognizes gp160 and its subunits and launches an attack against the molecules. Vaccine researchers are attempting to use recombinant gp160 to mimic that response in persons who have not been infected with HIV.

In a Phase I study now nearing completion, NIAID investigator Dr. Lane showed that high doses of the gp160-based AIDS vaccine manufactured by MicroGeneSys, West Haven, Connecticut, elicit immune responses against three HIV isolates. Antibody responses increased as vaccine doses were increased. Volunteers who received the vaccine experienced only minor side effects (local reactions, flu-like symptoms, and fever) and no serious toxicities. A Phase I multicenter study by the NIAID VEUs confirmed the safety of up to 80 micrograms of this gp160 subunit vaccine in a broad group of subjects.

NCVDG researchers studying SIV, a monkey virus closely related to HIV, reported that some monkeys injected with an experimental vaccine made from SIV and then exposed to the disease-causing virus were protected against a monkey version of AIDS. NIAID grantee Dr. Ronald Desrosiers and colleagues at the New England Regional Primate Center gave the animals a series of injections containing whole but inactivated SIV. When challenged with the live virus, two of the six vaccinated monkeys showed complete protection from infection. Researchers were unable to isolate virus from the animals' blood, suggesting that the animals were not infected at all. Also, blood from these monkeys failed to infect normal monkeys. Although the remaining four vaccinated monkeys became infected with SIV, three of them showed no signs of illness. The next step will be to study the chemical and biological changes that occurred in the immune systems of the monkeys that were protected by the vaccine.

Dr. Murphey-Corb and her collagues at the Delta Regional Primate Research Center have developed a vaccine that has protected monkeys from illness caused by SIV. Of the nine monkeys vaccinated, eight showed no signs of infection nine months after exposure to live SIV. Blood samples from the remaining vaccinated monkey showed evidence of infection, although the animal appears healthy. In contrast, all four unprotected control monkeys in the experiment have shown signs of infection and two have died. The vaccine contained SIV that had been chemically treated so that the virus could not cause disease. These results provide the most encouraging evidence so far that a vaccine to protect against human AIDS is indeed possible.

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International Studies Provide Assistance

To encourage studies of AIDS in foreign countries where epidemic numbers of people harbor HIV or suffer from the disease, NIAID awarded five grants for International Collaboration in AIDS Research (ICAR). These 3- and 5-year grants are enabling U.S. scientists to work with researchers in Africa, Mexico, and Brazil to investigate pressing AIDS-related health problems, uncovering valuable information about how cultural, geographic, and genetic differences influence the course of HIV infection. Additional ICARs are expected to be funded for projects in Asia, Southern Africa, and parts of the Americas, where high incidence of HIV disease is documented in at least a subset of the population.

The ICARs strengthen NIAID's ongoing commitment to international AIDS research. NIAID scientists are already involved in studies of AIDS in five African countries--Zaire, Kenya, The Gambia, and the Sudan. In addition, NIAID and the Pan-American Health Organization have established collaborative studies of AIDS in the Caribbean, where the disease is known to be widespread. To date, most Asian countries so have reported many fewer cases of AIDS than countries in the Americas, Europe, and Africa; however, NIAID has provided training, consultants, and reagents to the Indian government for studies among people at high risk for HIV infection.

Outreach Programs Developed for Broad Distribution of Information

NIAID is attempting to reach more minority health care workers and populations with information about AIDS. The institute has participated in and sponsored workshops and speakers at national meetings. At an NIAID National Advisory Council meeting, Dr. Margaret Hamburg, NIAID Assistant Director for Science Policy, outlined the institute's plans to intensify efforts and develop improved strategies to address the needs of minority persons with HIV infection as well as minority health professionals treating AIDS patients. Among NIAID minority initiatives in 1989 were presentations and an exhibit at the annual meeting of the National Medical Association, organization of a workshop for deans and educators at the National Black Nurses Association conference, organization of workshops and an exhibit at the third national conference on HIV infection among racial and ethnic populations, and an exhibit at the Fourth Hispanic Medical Congress.

To broaden the dissemination of information about clinical trials, in the past year NIAID, in cooperation with the Centers for Disease Control (CDC) and FDA, introduced the AIDS Clinical Trials Information Service (ACTIS). This

important innovation, a part of the coordinated PHS AIDS information initiative, is a computerized service that provides current information free of charge to physicians and other health practitioners, as well as to patients and their families. The toll-free service provides specific information about NIH-sponsored clinical trials of experimental therapies for AIDS and AIDS-related diseases and drug company-sponsored efficacy trials. The information, which is updated weekly, includes eligibility requirements, exclusion criteria, study location and duration, names and telephone numbers of contacts at each study site, and descriptions of specific experimental therapies under study. Spanish-speaking health specialists are available, and computer printouts of custom searches of the data base can be requested. All communication is completely confidential. ACTIS can be reached by dialing 1-800-TRIALS-A, or through the National Library of Medicine's online services.

To convey the most current information on AIDS research, including the latest accomplishments of the NIAID AIDS effort, NIAID's Office of Communications distributes Backgrounders and other materials. The Institute's Division of AIDS produces AIDS Research Exchange, a publication to inform AIDS researchers of new program and research developments.

To help physicians and other health professionals understand the purpose and process of clinical trials, NIAID is developing an AIDS Clinical Trials Education Module. Brochures targeted to different patient groups have been prepared as part of this effort. Eight NIAID-supported ACTUs in addition to their clinical trial and basic research activities, conduct outreach programs for AIDS education and technology transfer.

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NATIONAL CANCER INSTITUTE

The NCI conducts research on the basic biology of the human immunodeficiency virus, including mechanisms of infection, molecular biology, and immunology; develops drugs, vaccines, and biological therapies to prevent and treat AIDS; and studies patterns of occurrence of HIV infection and disease.

Pathogenesis of HIV Disease

NCI contractors Dr. Connie Faltynek, Louise Finch, and W. Roy Overton of Program Resources, Inc., Frederick, Maryland, along with intramural researcher Paul Miller, have reported that interferon gamma, a natural immunostimulant, decreases expression of the CD4 surface receptor on monocytes (a type of immune cell). On the basis of this finding, the researchers suggest that treatment of AIDS patients with interferon gamma might reduce the susceptibility to infection of their monocytes to infection. In their studies, Dr. Faltynek and her co-workers used biotechnology to produce a recombinant form of interferon gamma.

HIV-infected human cells produce viral messenger RNA (mRNA), which serves as a template for manufacture of viral proteins. Dr. George Pavlakis and colleagues at NCI's Frederick Cancer Research Facility (FCRF), have shown that the HIV regulatory protein "Rev" promotes transport of a subset of viral mRNAs from the nucleus to the cytoplasm and increases their half-life. Feedback regulation by Rev leads to a steady state of HIV production. Scientists hope to learn how to inhibit Rev function, thus blocking virus production. Using PCR, Dr. Pavlakis and his co-workers have identified more than 30 mRNAs produced in HIV-infected cells. For the first time, scientists now have an almost complete list of the different mRNAs produced by HIV.

Viruses as Cofactors in AIDS

Human herpesvirus type 6 (HHV-6) is a cytopathic (cell-damaging) virus with marked affinity for T-cells bearing the CD4 receptor (CD4-positive cells)--the same immune cells that are also prime targets of HIV-1. Moreover, majority of AIDS patients are infected with HHV-6. Intramural researchers Drs. Robert Gallo, Paolo Lusso, Barbara Ensoli, Dharam Ablashi, Erwin Tschachler, and Flossie Wong-Staal, along with Dr. S. Zaki Salahuddin of NCI, Dr. Phillip Markham of Bionetics Research, Inc. (BRI), Rockville, Maryland, under contract to NCI, and colleagues have demonstrated that HHV-6 and HIV-1 can co-infect individual human CD4-positive T-cells, resulting in accelerated HIV-1 expression and cell death. The scientists have also

presented direct evidence that HHV-6 activates HIV-1 by producing a factor or factors that bind to HIV-1 RNA and trigger the virus to replicate, and they have identified the precise portion of HIV-1 genetic material to which the factor binds.

These observations indicate that HHV-6 may play an important role in the progression of AIDS in some HIV-1 infected individuals, and that it may contribute to the depletion of CD4-positive T cells that is seen in AIDS.

HIV Genes and Proteins Identified as Potential Targets

The HIV integration protein (IN) is required for integration of the HIV provirus (HIV DNA) into the DNA of human cells, an essential step in the establishment of infection. Drs. Stephen Hughes and Amnon Hizi at BRI, under contract to NCI, have succeeded in inducing E. coli bacteria to produce IN and have begun efforts to purify the protein and prepare antibodies against it. Knowledge of the structure and activity of IN could prove helpful in designing drugs that would inhibit integration of the HIV provirus.

The enzyme reverse transcriptase plays a role in HIV infection through its ribonuclease or RNA-cutting activity. Intramural researchers Drs. Shelby Berger and Marc Krug have established that HIV ribonuclease is more sensitive than cellular ribonuclease to the structure of the RNA molecules it acts upon its substrates. This dissimilarity could be exploited for drug design, the researchers suggest, since it might be easier to inhibit the viral enzyme than its cellular counterpart.

Production of HIV involves the processing or modification of viral proteins so that they can function properly. One step in this processing is the splicing, or cutting, of the proteins with an enzyme called a protease. The HIV protease is an attractive target for the design of specific inhibitors to be used as antiviral agents. Before such inhibitors can be designed, however, it is necessary to understand the enzyme's structure.

Drs. Alexander Wlodawer and Maria Miller of BRI, under contract to NCI; Dr. Stephen Kent of the California Institute of Technology; and colleagues have now determined the crystal structure of the HIV protease. This structure differs in several important details from one reported earlier by another research team, but there is general agreement that the newly determined structure is the correct one.

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Kaposi's Sarcoma--New Factors Delineated

Intramural researchers Drs. Gallo, Ensoli, Wong-Staal, and Shuji Nakamura, along with Drs. Salahuddin of NCI and Peter Biberfeld of the Karolinska Institute in Stockholm, Sweden, have identified two well-known growth factors--basic fibroblast growth factor (bFGF) and interleukin 1 (IL-1)--that are produced by Kaposi's sarcoma (KS) cells from AIDS patients and that induce proliferation of KS cells. IL-1 is known to activate T cells, and bFGF induces growth of new blood vessels. The finding that these factors stimulate growth of KS is consistent with the hypothesis, proposed earlier by Dr. Gallo and colleagues, that a cascade of growth factors, or activities, is involved in early development of KS.

In nude mice (immunodeficient mice capable of accepting foreign tissue), KS cells from AIDS patients induce KS-like tumors of mouse origin. This result, along with the other findings, suggests that KS may develop as a reaction of normal cells to external growth factors, rather than a true cancer.

Animal Models Used in Vaccine Development

Most macaque monkeys used in medical research are infected with the simian AIDS (SAIDS) virus. This virus is less closely related to HIV than the less common SIV; nevertheless, it causes an illness that shares many characteristics with human AIDS.

Intramural researchers Drs. Raoul Benveniste and Gisela Heidecker; Dr. Shiu-Lok Hu of Oncogen in Seattle, Washington; Dr. Willam Morton of the Washington Regional Primate Research Center in Seattle; and their colleagues have demonstrated that a genetically engineered vaccine can protect macaque monkeys against SAIDS. The new vaccine combines part of the protein coat of the SAIDS virus with vaccinia virus, which acts as a carrier and as an immunostimulant.

This year, NCI researchers Drs. Jay Berzofsky and Gene Shearer; Dr. Richard Houghten of the Scripps Clinic and Research Foundation; Dr. Scott Putney of Repligen Corp., Cambridge, Massachusetts; Dr. R. Neal Boswell of Lackland Air Force Base in Texas; Dr. Charles DeLisi of Mt. Sinai Medical School, New York City; and colleagues have tested six regions of the HIV envelope protein gp160 as a vaccine in mice of four different tissue types. Each of the six regions successfully immunized either three or four of the four types of mice tested.

Four of the envelope regions identified in mice elicited responses in a large proportion of cells from HIV-

infected humans. Thus, in humans as well as animals, just a few HIV peptides may be sufficient to elicit immune responses in a large population of genetically diverse individuals. This finding is encouraging in view of concern that artificial vaccines containing only a few HIV antigenic sites might not be consistently effective in large populations.

Drug Development and Treatment Progress

In FY 1989, about 16,000 agents passed through NCI's large-scale screening program for candidate drugs for cancer and AIDS. In 1990, when the program is fully operational, more than 40,000 agents will be screened yearly. Already least 15 promising new classes of candidate antiviral agents have been identified. One or more of these new compounds may be available for clinical testing within the next one to two years.

In 1989, intramural researcher Dr. Michael Boyd and his colleagues at NCI and at Program Resources, Inc., under contract to NCI, published details of a simple, quantitative assay for high-volume screening of candidate agents for activity against HIV. The test's simplicity minimizes handling of HIV by laboratory workers, an important safety feature.

Intramural scientists Drs. Samuel Broder, Robert Yarchoan, Hiroaki Mitsuya, and colleagues reported results from a Phase I study indicating that ddI is active against HIV in AIDS and poor-prognosis ARC patients, and may, at certain doses, have little short-term toxicity. At the higher doses of ddI, patients showed decreased levels of virus in their blood, along with increases in immune cells. Most of the patients tolerated ddI without side effects, although high doses produced adverse effects in some patients. Large multi-institution Phase II clinical trials of this agent are now under way in NIAID's ACTG.

Preliminary results, reported by intramural scientists Drs. Robert Yarchoan, Samuel Broder, and colleagues, of a Phase I study of the recombinant soluble CD4 cell surface receptor suggested that rsCD4 may have reduced the load of HIV in a few patients with AIDS or poor-prognosis ARC. One difficulty with rsCD4 is that, because the drug is rapidly cleared from the body, it is not feasible to attain high levels in the blood. Second generation versions of rsCD4, such as hybrids combining rsCD4 with immunoglobulins, may alleviate this problem while enhancing the agent's antiviral effect. Several such rsCD4/immunoglobulin hybrids have been developed by Drs. Daniel Capon and Douglas Smith at Genentech, Inc., in South San Francisco; Drs. Mitsuya and Broder at NCI; Dr. Gerald Groopman at New England Deaconess Hospital in Boston; and their colleagues. Clinical trials

are now being conducted with AIDS patients at several medical centers, including the NIH Clinical Center.

Grantee Dr. Ellin Berman and colleagues at Memorial Sloan-Kettering Cancer Center, in collaboration with researchers at Harvard Medical School, conducted laboratory studies on the bone marrow toxicity and anti-HIV activity of AZT and alpha interferon used as single agents and in combination. Their results (like those of NIAID's Drs. Fauci and Lane) suggest that AZT and alpha interferon may act synergistically against HIV. Such an effect might make it possible to lower the doses of both substances, thereby limiting bone marrow toxicity.

Intramural researchers Drs. Philip Pizzo, David Poplack, Frank Balis, and colleagues, studying children with AIDS, have found that continuous infusion of AZT is superior to an intermittent schedule of drug delivery. Continuous infusion permits the patient to receive lower total daily doses of the drug while still maintaining a high enough blood level to inhibit HIV activity. With continuous infusion of AZT, the researchers found children with impaired neurodevelopmental function improved dramatically. They regained skills such as walking and talking, and school-aged children showed significant improvement in their intellectual functioning.

Epidemiology Studies Provide Clues to Disease Development and Progression

This year, intramural researchers Drs. James Goedert and Mitchell Gail, Drs. M. Elaine Eyster and James Ballard of the Pennsylvania State University School of Medicine in Hershey, and colleagues reported on a more precise way of determining whether an HIV-infected hemophiliac will soon develop AIDS. The investigators found that high levels of the HIV p24 antigen and low counts of CD4-positive T cells are strong predictors that the disease will develop.

In infants born to women infected with HIV, premature birth or low levels of maternal antibodies against the gp120 envelope protein of HIV may be indicators of risk for AIDS. This research was conducted by intramural researcher Dr. Goedert; Dr. Sheldon Landesman at the State University of New York Health Science Center in Brooklyn; Dr. Anne Willoughby at the NICHD; Dr. Roy Stevens at the New York State Department of Health in Albany; Dr. Arye Rubinstein at Albert Einstein College of Medicine in New York City; Mr. James Drummond at Program Resources, Inc., under contract to NCI; and their colleagues.

In as much as infants born to women who lacked anti-gp120 HIV antibodies were at high risk of being infected, it is possible that levels of anti-gp120 could

serve as an early marker of infection in these infants. Potentially, antibodies to gp120 could also be used as a treatment to neutralize HIV. In addition, vaccines made from portions of the gp120 protein might offer protection to infants born of infected mothers.

A new analysis has been completed on cohorts of homosexual men that NCI has been studying for AIDS risk since 1982. The study was reported by intramural scientists Drs. Goedert, Alexander Kramer, Philip Rosenberg, Robert Biggar, and William Blattner, along with Dr. Dietmar Fuchs of the Universitat Innsbruck, Dr. Sheldon Milstien of the National Institute of Mental Health, and colleagues. The researchers identified two serological markers that are predictive of progression to AIDS. High levels in the blood of a substance called neopterin indicate a high AIDS risk some 3 years before diagnosis. Beta-2-microglobulin levels become predictive in the year before AIDS diagnosis.

Currently, there is still great uncertainty about the number of persons infected with HIV. A new method called "back calculation" of HIV infection has been refined, tested, and simplified by intramural researchers Drs. Rosenberg and Gail and their colleagues. Back calculation incorporates knowledge of AIDS incubation time in estimating the numbers of persons infected with HIV. Preliminary results obtained using this method suggest that 1 million persons in the United States were infected with HIV by the spring of 1988. This estimate is consistent with the results of CDC surveys in special populations.

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NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

NHLBI supports research on AIDS in the areas of transfusion safety, blood diseases, and pulmonary and cardiac complications of HIV infection.

New Methods Increase Sensitivity and Specificity of Pretransfusion Testing

Dr. Girish Vyas, an NHLBI contractor at the University of California, San Francisco, has developed a sensitive and specific test that uses a flow cytometer (an instrument capable of detecting cells bound to fluorescent-labeled antibody) to detect the presence of antibody to HIV. In his test, polystyrene beads of various sizes are coated with different HIV proteins (p24, p31, gp41, and gp120) capable of binding any HIV antibody in the test specimen. After test specimen is mixed with the beads, fluorescent-labeled immunoglobulin reveals the presence of HIV antibody by binding to HIV-antibody complexes. When tested in 126 coded blood samples, this method proved more sensitive and more specific than currently licensed HIV antibody tests.

Another NHLBI contractor, Dr. Robert Yolken at the Johns Hopkins University, is adapting PCR technology for use in the clinical laboratory and blood bank settings. Dr. Yolken has developed an assay that combines the high sensitivity and specificity of PCR testing methods with the technical conveniences of the currently used enzyme immunoassay systems.

With a similar assay using labeled HIV DNA probes, Dr. Robert Singer, a contractor at the University of Massachusetts in Worcester has successfully detected single infected cells in cultured lymphocytes as quickly as 12 hours after infection. This extremely sensitive technique not only detects HIV DNA sequences but also provides a rapid assessment of viral protein synthesis within individual cells. The assay was used to detect HIV protein in 436 cell culture samples obtained from 60 seropositive patients. The sensitivity and specificity of the hybridization assay were 93.5 percent and 94.6 percent, respectively.

Dr. Bernard Poiesz, a grantee at the State University of New York, Syracuse, developed a procedure capable of distinguishing HIV RNA from HIV DNA by the PCR assay. This distinction is important because defective replication of the HIV genome so frequently results in the formation of DNA incapable of replicating and producing infection. An assay capable of detecting the presence of RNA would indicate whether the virus is actively replicating, knowledge that would be useful for planning therapy and gauging its effectiveness. In Dr. Poiesz's procedure, test samples are preincubated with RNase-free DNase to digest any DNA

sequences present and ensure that only RNA will be detected. After a cDNA copy of the RNA is made by adding reverse transcriptase, RNA is amplified. Possible clinical applications of this test are being studied.

Dr. Robert Ting, a contractor at Biotech Research Laboratories, Rockville, Maryland, has developed a simple test that can be used for detection of antibody to HIV-1 in those parts of the world that lack sophisticated laboratory equipment necessary to perform currently available tests. Dr. Ting's test uses a nitrocellulose dipstick that changes in color intensity when exposed to samples of blood containing HIV antibody. The dipstick results, are available in 90 minutes and are not dependent on instrumentation. There was good correlation between the ELISA results and the visual color assessments for HIV antibody. False positives occurred, but no more than in most solid phase immunoassays.

Current Screening Tests Ensure Relatively Small Risk of Transfusion-Transmitted HIV-1

Several studies have been funded by the NHLBI to assess the current safety of the blood supply by determining how frequently HIV-1 infection is transmitted by transfusion of seronegative blood (i.e., blood that tests negative for the virus).

The rates of infection with both HIV-1 and human T-lymphotropic virus type I (HTLV-I) in a group of heavily transfused adults undergoing cardiac surgery were determined by Dr. Kenrad Nelson, a contractor at the Johns Hopkins University. More than 4,000 patients, all of whom were seronegative before surgery, received a total of 36,282 transfusions of blood components screened for HIV-1 but not for HTLV-I. One case of HIV-1 infection was attributed to transfusion of seronegative blood components. Among the 2,749 patients tested for HTLV-I, who had received more than 20,000 units of blood components, five new cases of HTLV-I infection were identified. The risk of HIV-1 transmission by transfusion was 0.003 percent per unit whereas the risk of HTLV-I transmission was 0.024 percent per unit--nearly ten times greater. This study indicates the desirability of screening for HTLV-I.

Dr. James Mosley, a contractor at the University of Southern California, Los Angeles, is assessing the sensitivity and specificity of tests that detect HIV-1 p24 antigen and is comparing the results with those of the antibody tests currently used in pretransfusion screening. Of 25,892 sera collected in late 1984 through early 1985 in the San Francisco area, 2,297 sera from high-risk areas were tested using the ELISA and Neutralization reagents. Although the anti-HIV antibody prevalence in this group was 1.08 percent, no donations positive for HIV p24 antigen were

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detected. This result calls into question the need for adding antigen testing to the pretransfusion screening process.

Progress Achieved in Removing and Inactivating Viruses in Blood and Blood Products

Because blood screening procedures are not entirely effective in preventing the transmission of HIV-1, NHLBI has been supporting the development of procedures that utilize heat or chemicals to inactivate retroviruses in donated blood. These procedures appear to be effective in destroying HIV-1 in blood derivatives such as Factor VIII and Factor IX preparations, but blood components such as cryoprecipitate, which is a source of Factor VIII, red cells, and platelet components, do not tolerate heat treatment.

Dr. David Bing, a grantee at Tufts University Medical Center, Boston, investigated the effectiveness of filtration procedures that remove virus-infected leukocytes from blood and chemical procedures that inactivate HIV-1. Units of blood infected with either HIV-1 or HIV-2 were processed through three bands of leukocyte-removal filters, then the lymphocytes were then cultured to determine thir infectivity. It was established that more than 99.5 percent of the cell-associated virus was removed by the filters. Antiviral activity was determined also for various chemical inactivating agents including propanol, chlorbutol, and LP1. LP1 completely inactivated HIV isolates that contained lymphocytes from a seropositive donor. Further characterization of LP1's antiviral activity is in progress.

Persons With Transfusion-Transmitted HIV Infection Continue Heterosexual Contacts

The potential for heterosexual transmission of HIV by individuals with transfusion-associated HIV infection was assessed by Dr. Mosley and his colleagues at the University of Southern California, Los Angeles, contractors for the NHLBI Transfusion Safety Study. A total of 522 HIV-1 antibody-positive subjects likely to have been infected by transfusion of blood components or clotting factor were questioned regarding their sexual behavior. Seventy-one percent reported having sexual contacts after being informed of their infectivity. Of those, twenty-three percent reported that they were sexually active with multiple partners. Thus, there is the potential for heterosexual transmission by individuals with transfusion-transmitted HIV infection.

Animal Models Elucidate Factors Underlying Clinical Expression of AIDS

The chimpanzee is one of the few animals besides man that can be infected by HIV-1. Despite their susceptibility to infection, however, chimpanzees fail to demonstrate any symptoms related to infection with the virus. Dr. Vyas, a grantee at the University of California, San Francisco, studied HIV infection in the chimpanzee to determine the reasons for this apparent lack of clinical expression of the virus. Of six chimpanzees seropositive for HIV, Dr. Vyas has found that none developed any immunologic abnormalities. One clue to the chimpanzee's "natural" resistance to the pathologic effects of HIV may lie in its CD8 lymphocytes (white cells that carry a cell surface receptor, known as CD8, which is analogous to the CD4 receptor). In contrast to CD8-positive cells in seronegative people, CD8 lymphocytes from uninfected control chimpanzees have shown antiviral activity.

Initial Findings on Cardiac Manifestations of HIV Infection Presented

In June 1989, six different groups of NHLBI-supported investigators presented their findings on the cardiac manifestations of HIV infection. Dr. Ahvie Herskowitz, a grantee from The Johns Hopkins University, reported transient cardiac dysfunction in AIDS patients demonstrated by echocardiography (a procedure that uses ultrasound to look at the heart). Dr. William Lewis, a grantee from the University of California at Los Angeles, detected HIV in the cardiac tissue of one patient, but the extent to which HIV infection itself can cause heart disease has yet to be determined.

Dr. John Craighead, a grantee from the University of Vermont, found that cytomegalovirus (CMV) could replicate in the cells lining the blood vessels (endothelium) and in the supporting tissue, but could not replicate in cardiac muscle cells. In mice, six strains of CMV have been studied. Some strains produce a diffuse inflammation in the cardiac muscle, whereas other strains cause lesions only in the presence of immunologic suppression.

Dr. Alan Ross, a grantee from George Washington University, Washington, D.C., found that 68 of 80 patients infected with HIV demonstrated high titers of antibodies to cardiac tissue, indicating that much damage could be due to autoimmunity. Dr. Lewis also reported cardiac lesions suggesting an inflammatory process involving the small blood vessels.

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Intramural Researchers Focus on Genetic Approaches to Blocking and Inactivating HIV Infection

Viruses containing the gene for the soluble form of the T-cell receptor site for HIV (sCD4) have been developed by NHLBI intramural researcher Dr. French Anderson and used as vector to transfer this genetic material to other cell lines. Dr. Anderson showed that sCD4, which competitively inhibits binding of virus to the CD4 receptor on the lymphocyte, could protect cells from infection by HIV. These findings may lead to a model for gene therapy in the treatment of AIDS by eventually inserting this gene into the cells of infected individuals so they may continually produce sCD4 to protect uninfected cells.

NHLBI intramural scientist Dr. Rodney Levine is working to develop agents containing free radicals, highly reactive substances that can inactivate enzymes and nucleic acids essential for HIV replication. Preliminary studies have involved the production of DNA capable of binding to a nucleic acid in an HIV gene that is essential for virus replication. This DNA splits the nucleic acid at the target site so that the gene is no longer intact. Research in this area has been limited, however, by in sufficient quantities of HIV-related proteins, so considerable effort is now being devoted to the production of these proteins by recombinant techniques.

NATIONAL INSTITUTE OF DENTAL RESEARCH

NIDR is conducting basic, clinical, and epidemiological research on AIDS directed toward improving treatment and ultimately preventing oral lesions associated with HIV infection.

HIV Found in Oral Fluids

Drs. Patricia A. Murray and James R. Winkler at the University of California at San Francisco have discovered the HIV virus in inflammatory fluid drawn from infected gums of HIV-positive patients. Using a recently developed genetic probe, these NIDR grantees were able to detect the virus in gingival crevicular fluid as frequently as they found the virus using the standard blood test in the same patients. A high percentage of HIV-infected patients suffer from acute, painful, and rapidly destructive periodontal disease characterized by sore and bleeding gums and severe soft tissue damage. Additional studies are under way to determine whether the presence of HIV in oral fluids indicates a role for these fluids in the transmission of the virus.

Following up on these findings, Dr. Robert Genco and colleagues at the State University of New York at Buffalo explored differences in the oral flora between two groups of AIDS patients--homosexuals and intravenous drug users. Using an immunofluorescence technique, these NIDR grantees found that bacteria common to periodontal diseases predominated in the homosexual group while bacteria common to caries predominated in the drug users. These results suggest that the high prevalence of HIV-associated periodontal disease in homosexual AIDS patients may be due to the specific composition of dental plaque.

Basic Studies Home in on AIDS Pathology

Researchers in the NIDR intramural laboratories are focusing on AIDS-related dysfunctions of the immune cells known as monocytes. Applying the tools of biotechnology, Drs. Sharon Wahl and Phillip Smith have shown that monocytes infected by HIV-1 undergo premature differentiation and are no longer able to respond to normal immunologic stimuli.

Advances also have been made in the development of animal models for AIDS. Transgenic mice have been created that bear all or some of the HIV genes stably incorporated in their genomes. Several of these mice manifest AIDS-related pathology, creating models for studying juvenile AIDS and HIV-associated kidney disease. These animals will be a valuable resource for learning about the progression of AIDS and for testing protocols for disease intervention.

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Saliva Protects the Oral Tissues

Dr. Earl J. Bergey, an NIDR grantee at the State University of New York at Buffalo, has demonstrated in cell cultures that certain components of saliva can neutralize herpes simplex virus-I, which causes an opportunistic infection associated with AIDS.

In addition, NIDR intramural scientists Drs. Philip Fox and Jane Atkinson confirmed previous observations that salivary secretions from infected men, women, and children inhibit HIV activity. Saliva is one of the main defense mechanisms in the oral cavity, and alterations in salivary function and composition may play a role in oral changes associated with HIV. Drs. Fox and Atkinson have reported specific changes in salivary gland secretions in humans infected with HIV, demonstrating for the first time that salivary glands are affected by HIV. In HIV-infected individuals followed over time, these changes become more extensive.

HIV Delays Tooth Eruption in HIV-Infected Offspring

Results from a 3-year study of children born to mothers at high risk for HIV infection, conducted by grantee Dr. John Greenspan and colleagues at the University of California at San Francisco, show that these children are susceptible to delayed eruption of teeth and abnormal patterns of tooth eruption. Based on these preliminary data, further investigations are warranted to explore the effects of pediatric HIV infection on tooth development and to find ways to prevent or treat these problems.

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

NIDDK conducts and supports research on AIDS, much of it concentrating on understanding the basic mechanisms of this devastating viral disease.

New Compound Could Cross Blood-Brain Barrier

NIDDK scientist Dr. Paul Torrence has synthesized and is evaluating three new derivatives of dideoxycytidine (ddC) which are designed to cross the blood-brain barrier, a tightly knit network of capillaries that helps protect the brain from chemical invaders. Although ddC has been shown to have anti-HIV activity in culture and in clinical trials, its therapeutic value is limited because it cannot penetrate the brain, which often harbors the AIDS virus. To date, syntheses and pharmacological studies on ddC derivatives designed to cross the blood-brain barrier have been hampered by the chemical instability of the drugs. Dr. Torrence and his collaborators have developed techniques to assess accurately the action of these compounds once in the blood and brain and are now using these techniques in studies with rats. They hope to discover if these new ddC compounds can cross the blood-brain barrier without losing their anti-HIV properties.

Possible Mechanism of Platelet Underproduction Found

NIDDK grantees Drs. Dorthea Zucker-Franklin and Yunzhen Cao at New York University Medical Center in New York City have found that HIV may directly infect megakaryocytes, large cells in the bone marrow that release mature blood platelets. Previous studies yielded no such evidence of direct HIV infection; abnormalities seen in megakaryocytes were thought to be caused by other immune cells known to be infected by the AIDS virus. This finding may help explain why some AIDS patients have a severely lowered level of blood platelets, a condition called thrombocytopenia.

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THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Clinical surveys have detected neurological complications in about 40 percent of adult AIDS patients. Postmortem studies, however, put that figure as high as 80 percent. This neurological damage can be caused directly by HIV or result from a secondary opportunistic infectious agent, and may affect the central or the peripheral nervous system. Occasionally, nervous system damage is the only symptom of AIDS infection, often in its earliest phases.

Defining AIDS Dementia

Several NINDS-supported research projects are under way to define and describe AIDS dementia, a disorder found in as many as 40 percent of AIDS patients. NINDS grantee Dr. Richard Price at the University of Minnesota in Minneapolis is working to correlate the location of HIV in the brain of AIDS patients with the development of AIDS dementia. Dr. Price is also evaluating the effectiveness of positron emission tomography (PET), a brain imaging technique, as a diagnostic tool in AIDS dementia by comparing PET results with those from conventional neuropsychological tests. His studies have shown that AIDS dementia patients in the early stages of the disease have abnormally high levels of glucose metabolism, a measure of brain activity, in those brain areas most often infected by HIV. However, the scans have also revealed that glucose metabolism becomes generally depressed as AIDS dementia progresses, indicating a slowdown in brain activity.

In another study, NINDS grantee Dr. Leroy Sharer of the University of Medicine and Dentistry of New Jersey in Newark identified abnormalities in brain blood vessels of children with HIV-associated inflammation of the brain. Dr. Sharer also determined that these changes occurred mostly in specific brain areas and were rare in adult cases. His findings suggest that AIDS dementia in children may differ in both its origins and its symptoms from the adult form.

Exploring How HIV Damages the Nervous System

Despite the prevalence of neurological involvement following HIV infection, it is unclear why this infection's effect on the nervous system varies widely from one patient to another. However, it is known that HIV mutates rapidly, producing many strains. Because studies have shown that one patient can harbor several strains of HIV, scientists have hypothesized that various strains of the virus may be responsible for the nature and extent of neurological damage seen among different patients. With support from the NINDS, Dr. Cecilia Cheng-Mayer at the University of California, San Francisco, has shown that different strains of HIV have a predilection for specific cells. For example, virus

isolated from the brain reproduces more quickly in macrophages, a type of immune cell, while blood isolates replicate faster in T cells.

HIV Also Affects Muscles

NINDS intramural scientist Dr. Marinos Dalakas has identified abnormal muscle conditions called myopathies in AIDS patients. It is not known if these myopathies result directly from HIV or are caused indirectly by HIV-induced immune abnormalities. However, recent research by Dr. Dalakas, using labeled antibodies that seek out and mark the virus, showed that HIV is present in macrophages found in the muscles of AIDS patients. Dr. Dalakas is now searching with still more sensitive techniques to determine if HIV is also present in the muscle fibers of these patients.

Monkey Model Developed

NINDS intramural scientist Dr. Maneth Gravell has developed a monkey model for AIDS that shows great potential for providing information about the syndrome's neurological aspects. In his study, rhesus monkeys were inoculated with a strain of simian immunodeficiency virus (SIV). Three of the six monkeys developed AIDS-like symptoms, such as chronic wasting, diarrhea, and abnormalities of the lymph nodes. Significantly, these three monkeys also exhibited neurological problems, including impaired motor function and physical abnormalities in the brain. In addition, Dr. Gravell isolated virus from the brain, spinal cord, spinal fluid, and peripheral nerves and muscles of the infected animals. Dr. Gravell plans further studies of this model to probe for insights into the effects of HIV on the nervous system and the mechanism of infection in neurological AIDS.

New Vaccine Shows Promise

NINDS intramural scientist Dr. Clarence J. Gibbs has conducted experiments to test a potential AIDS vaccine in chimpanzees, with promising early results. In his study, three animals were inoculated with a whole killed HIV virus vaccine. Two of these chimps were already infected with HIV; the third was uninfected. A fourth animal--uninfected and unvaccinated--served as a control. All four animals were then inoculated with live virus. The control animal and the previously uninfected but vaccinated animal became infected with HIV. But the two vaccinated and previously exposed chimpanzees were no longer viremic, that is, despite repeated attempts, scientists could not isolate HIV from their blood. Thus, the vaccine appears to confer resistance to re-infection with HIV and has potential for preventing development of AIDS in infected asymptomatic humans.

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NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

In the hope of ameliorating the AIDS epidemic, scientists from diverse medical disciplines are seeking treatments for the disease. But basic research on the fundamentals of cell function must also be vigorously pursued if this illness is to be conquered.

One researcher whose long-time study of normal cell actions is now advancing the fight against AIDS is Dr. Melvin Simpson, an NIGMS grantee at the State University of New York at Stony Brook. He is studying AZT, which provides some benefits against AIDS, but also has dangerous side effects. Dr. Simpson has not only provided insights into why AZT is toxic to normal cells, he also has identified substances that act like AZT but that may be less toxic to uninfected cells and so might have potential as AIDS treatments.

Dr. Simpson has found that AZT toxicity may arise, not in the nucleus, but rather in cell organelles called mitochondria, which make the energy-containing compounds the cell must have to function. Because this energy is so crucial, even relatively minor impairments of the mitochondria can be lethal to the cell. Mitochondria are unique among cell organelles in that they contain a small amount of DNA. Like nuclear DNA, mitochondrial DNA undergoes replication. In fact, the enzyme that links nucleotides during mitochondrial replication was discovered by Dr. Simpson in the late 1960's. This mitochondrial enzyme is different from the one that performs a similar function in the nucleus. Could it be, Dr. Simpson wondered, that the mitochondrial enzyme, like the HIV enzyme, incorporates AZT during replication?

To test this theory, Dr. Simpson exposed isolated mitochondria to AZT and to 11 other nucleoside analogues. He found that AZT was one of the most potent inhibitors of DNA replication, and thus probably was being readily incorporated into the mitochondrial DNA. Although this finding suggests how AZT might kill cells, it does not answer the question of why bone marrow cells are so much more susceptible to the drug than other cells. Dr. Simpson is now attempting to answer this question using mouse leukemia cell cultures, which can mimic human bone marrow cells.

Explorations of mitochondrial DNA made by Dr. Simpson and his colleagues over the past two decades laid the groundwork for these recent efforts to seek less toxic AIDS therapies among nucleoside analogues. Their work is an excellent example of how sustained basic research plays a critical role in advancing medical science.

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

AIDS has become a significant cause of death in children and young people in the United States. Moreover, AIDS in children has some unique features. NICHD's AIDS related-research is focused on investigating the extent of the AIDS epidemic in women, infants, children, and adolescents; the transmission of the AIDS virus from mother to child; HIV disease treatment; ways to better understand the behaviors and attitudes that contribute to the spread of AIDS; and methods to prevent the sexual transmission of the AIDS virus.

Perinatal Infection Studies Expanded

Currently, the primary route of AIDS infection in children is from infected mother to child, and NICHD has undertaken a number of research projects related to HIV infection in infants, children, and mothers. One study, which is conducted jointly by a number of university-based researchers along with Dr. Anne Willoughby at NICHD and Dr. James Goedert at NCI, is assessing the impact of HIV infection on pregnancy outcome. The rate of so-called vertical transmission from infected mothers to offspring will also be determined.

NICHD continues to support the State Laboratory in the State of Massachusetts, which is screening routinely collected paper-absorbed samples of neonatal blood for the presence of HIV antibody. The samples come from the northeastern United States and North Carolina. These data will allow estimates to be made of the prevalence of HIV infection in childbearing women in these states and of the number of children who are being born with infection.

NICHD has also made six awards to investigators who will examine ways to improve the reliability and validity of methods of early diagnosis of HIV infection in infants, and to develop new methods of diagnosing vertically transmitted HIV infection early in life. This early diagnosis is crucial to the effective targeting and testing of therapeutic agents aimed at impeding the transmission of HIV infection from mother to child and at delaying the onset of symptomatic disease in infected, asymptomatic infants.

Effect of Pediatric AIDS on Developmental Outcome

Pediatric AIDS is known to affect the central nervous system, and clinicians have reported finding HIV-related CNS symptoms in babies just a few months old. A study headed by Dr. Joan Hittelman at the State University of New York Health Sciences Center at Brooklyn is looking specifically at the neurologic development of children with HIV

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infection. This study will follow the natural history of the disease in infected children, and will examine the impact of HIV on the neurodevelopmental outcome of their children.

Hemophilia and AIDS -- Natural History of Infection

Dr. Edward Gomperts at Children's Hospital of Los Angeles is heading a study to follow the natural history of HIV infection in hemophilic children. Children with hemophilia, who have contracted HIV infection from blood products, generally are older than most pediatric AIDS patients when diagnosed. In this study, which is conducted in coordination with NICHD's Dr. Willoughby, hemophilic children who are seropositive for HIV infection, together with seronegative hemophilic controls and seronegative nonhemophilic sibling controls, will be followed over a 4-year period. Investigators will assess their growth and neurologic development, immunologic status, and progression of the infection. This study is being conducted in coordination with the Health Resources and Service Administration, HRSA and the CDC.

Information and Education Program for Pediatricians

In an effort to reach children at an early age and to involve their parents, the NICHD has contracted with the American Academy of Pediatrics to design, implement, and evaluate a program to educate pediatricians in AIDS and human sexuality issues so that they, in turn, can convey the information to patients and parents.

Treatment for Children

Under the direction of Drs. Heinz Berendes and Anne Willoughby, NICHD has launched a 28-center study designed to assess the safety and efficacy of treating HIV-infected, symptomatic children with intravenous gamma globulin. This study will determine if such treatment reduces the occurrence of serious bacterial infections and death, slows the progression of HIV disease, of prevents other problems related to HIV disease. More than 300 children have been enrolled in this study to date. While not a cure for AIDS, treatment with IV gamma globulin may lengthen and improve the children's lives.

In response to a directive issued jointly by NICHD Director Dr. Duane Alexander and NIAID Director Dr. Anthony Fauci, the pediatric clinical trials centers supported by NIAID and the clinical trials centers supported by NICHD will work together in conducting research into effective ways of treating HIV infection in infants, children, adolescents, and pregnant women. This joint effort will markedly increase the number of pediatric and obstetric

subjects available for enrollment into state-of-the-art therapeutic research programs.

Research on Heterosexual Transmission of HIV

The NICHD and the U.S. Agency for International Development continue to support research conducted and sponsored by Eastern Virginia Medical School, where the heterosexual transmission of simian AIDS is being studied in the rhesus monkey. Female monkeys are partially protected against vaginal transmission of HIV by currently marketed spermicidal foams that contain nonoxynol-9. This research is being expanded in order to study the effects of different formulation of drugs. Other animal models are being assessed for their utility in studies related to contraception and HIV transmission.

NICHD continues the screening of compounds for both spermicidal and anti-HIV activities. The data are quite convincing that both spermicides such as nonoxynol-9 and others like benzalkonium chloride are very potent *in vitro* anti-HIV agents. Such information is critical for the design of new spermicidal formulations. It has been suggested that adding a known antiviral agent to currently available spermicides may provide additional protection against the heterosexual transmission of HIV. This concept is undergoing *in vitro* studies; if results are positive, it will be studied in animal models.

The Institute has reviewed a number of proposals received in response to a Request for Proposals soliciting research on development of condoms from materials other than latex rubber. It is anticipated that projects dealing both with the design of new condoms and clinical testing of new products will be initiated.

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NATIONAL EYE INSTITUTE

Of the opportunistic infections that threaten the sight of AIDS patients, cytomegalovirus (CMV) retinitis is the most common. In 15 to 45 percent of AIDS patients, CMV progressively destroys the retina, causing severe visual impairment and blindness.

Two drugs have shown promise in reducing or halting visual loss in AIDS patients: ganciclovir, the only drug approved by the FDA for the treatment of CMV retinitis, and foscarnet, an investigational drug which has not been as widely studied as ganciclovir. NEI scientists have found that ganciclovir when used alone is most effective against CMV retinitis at dosages that can cause dangerously high toxicity. Because ganciclovir and AZT, the only drug proven effective in prolonging life in AIDS patients, suppress bone marrow, they cannot be used together at the standard dosages. Foscarnet does not suppress bone marrow, so theoretically it could be used with AZT; however, foscarnet may cause kidney damage and must be discontinued when major kidney toxicity occurs. NEI scientists believe the best way to compare objectively the risks and benefits of these drugs is in a multicenter randomized clinical trial.

Beginning in January 1990, NEI-funded investigators at 12 clinical centers will begin recruiting 240 AIDS patients with CMV retinitis in one or both eyes for the Foscarnet Ganciclovir Retinitis Trial (FGRT). This is the first major randomized clinical trial to compare these two drugs. The objectives of the FGRT are to: 1) compare the safety and efficacy of foscarnet and ganciclovir for treating CMV retinitis in AIDS patients, 2) determine the effects of treatment on patient survival, and 3) compare the benefits of immediate versus delayed treatment with foscarnet or ganciclovir in patients with milder retinitis.

CMV lesions in the posterior retina are considered a more serious threat to sight because this part of the retina includes the macula, which provides sharp, central vision. Therefore, the first group will include patients with either posterior retinitis or extensive peripheral retinitis. These patients will be randomized to immediate treatment with either foscarnet or ganciclovir. The second group will include patients with milder retinitis confined to less than 50 percent of the peripheral retina. These patients will be randomized to receive either immediate or deferred treatment with foscarnet or ganciclovir. However, patients in the deferred treatment group will be offered drug treatment if their retinitis becomes sight-threatening.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

NIEHS is in a unique position among research organizations to evaluate the toxicological properties of promising AIDS antiviral agents, immunomodulators, and possible vaccines. As new treatment regimens enhance survival time for AIDS victims, it will become increasingly important to understand the toxicological side effects of such therapy.

Intramural scientists Drs. Michael Luster and Gary Rosenthal and their collaborators are studying the potential adverse effects of promising AIDS therapeutics on the immune and bone marrow systems. AZT is toxic for bone marrow. The scientists found that, in addition to inhibiting the formation of colonies of cells in the bone marrow, AZT also altered the stromal cell microenvironment. This observation may have clinical significance in HIV-positive but symptom-free individuals receiving AZT because long-term depletion of the stromal microenvironment can, in certain instances, damage the bone marrow's pool of progenitor cells.

Toxicity studies on pentamidine, an effective therapeutic agent against PCP, have focused on the drugs adverse effects on the function of macrophages in the lung. Therapeutic doses of the drug have been found to significantly suppress macrophage secretory products, but, without a concurrent suppression of other parameters of functions such as hydrogen peroxide production. Studies are in progress to determine the mode of action of this drug on macrophage function.

Dr. June Dunnick, NIEHS scientist, and her collaborators are studying the toxicity of AIDS drugs, particularly toxicity of combination therapies. These studies include an evaluation of general toxicity as well as neurotoxicity, toxicity to the hematologic system, and screens for reproductive toxicity and teratogenicity. Comparative data have been obtained on the hematologic toxicity of AZT and ddC, and a study is now under way to see if a variety of AZT/ddC combinations can reduce toxicity.

The mouse has been found to be more sensitive than the rat to AZT hematotoxicity. Hematotoxicity is seen at dose levels that correspond to human dose levels, indicating that this animal model should be a good system to use in predicting toxicity from antiviral agents. NIEHS and FDA have worked together to develop a set of 4-week studies to assess toxicity in rodents, including effects on cytokines.

The teratogenic potential of nucleoside drugs, including ddC and ddI, is also being studied. These studies are designed to obtain baseline toxicity data on the first generation of AIDS therapies and to evaluate the relationships between toxicity and chemical structure.

NATIONAL INSTITUTE ON AGING

Although most AIDS victims are in younger age groups, the disease affects a large number of middle-aged and older adults. In fact, 10 percent of all AIDS cases reported since the start of the epidemic have involved people aged 50 and over. By 1992 the total number of AIDS cases in adults over 40 years old will approach 100,000; and for those aged 60 and over, the number may reach 10,000.

Immune Functions in Older Persons with AIDS

Dr. William H. Adler of NIA's intramural program at the Gerontology Research Center in Baltimore is currently studying the course of the illness, the response to AZT therapy, and the changes in immune status in individuals with AIDS who are over age 60. Older persons with AIDS survive a shorter length of time following infection with HIV than do younger persons. This shortened survival for older patients was originally believed to be related to how the infection occurred, that is, in many cases through contaminated blood transfusions rather than other modes of infection. However, this has not proven to be the case since all older patients demonstrate a shortened survival period regardless of how they became infected. In an attempt to understand why older individuals react differently to HIV infection, the study focuses not only on AIDS but also on the decline of the immune system that occurs with advancing age. As a result of this decline, older people become more susceptible to infectious illnesses, and are more likely to die from these infections. Thus, at a time in life when older people are already developing an age-related immunodeficiency, HIV infection further compromises immune function, and the disease progresses more rapidly.

Publication of NIA Sourcebook on AIDS in Older Persons

A sourcebook, AIDS in an Aging Society,* was recently compiled by the staff of NIA's Behavioral and Social Research Program. The volume discusses issues and presents data concerning the AIDS epidemic, and addresses the common misconception that the epidemic represents no threat to people over age 50--a notion that has led people to assume prevention efforts are wasted on middle-aged and older people. It also marks the rapidly growing need for health care facilities for AIDS patients of all ages, a need that will intensify as people with AIDS begin to compete with

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*Riley MW, Ory MG, Zablotsky D, eds. AIDS in an Aging Society: What We Need to Know. New York: Springer Publishing Company, 1989.

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disabled older adults for long-term care resources, which are already in short supply. The books chapters were written by researchers throughout the United States who are studying AIDS and aging processes. The book is addressed to social and behavioral scientists involved in research, professionals in practice, and public policy makers who are concerned with the far-reaching implications of AIDS for people of every age.

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

Reports in the literature have continued to emphasize the occurrence of rheumatic, musculoskeletal, and skin manifestations in HIV-infected individuals. Rheumatic manifestations include reactive arthritis, Reiter's syndrome, psoriatic and infectious arthritis, inflammatory conditions of muscle, vasculitis and Sjogren's syndrome. Skin disorders include psoriasis, folliculitis, seborrheic dermatitis, molluscum contagiosum, and Kaposi's sarcoma.

Dr. Madelaine Duvic, an NIAMS-supported researcher in the Department of Dermatology at the University of Texas Medical School, Houston, reported that AIDS is associated with a more severe form of psoriasis than that seen in individuals not infected with HIV. Furthermore, a subsequent report by Dr. Duvic and colleagues suggested that AZT improves the psoriasis in patients with AIDS. These findings have since been confirmed by other investigators.

In another advance, Dr. Duvic and associates presented data indicating that PCR enables exquisitely sensitive detection of HIV in skin graft tissue. The use of skin grafts to cover wounds in severely burned patients has been recommended as an effective and safe therapy; however, HIV has been transmitted in engrafted tissues, and the HIV status of the donors or grafts may be unknown or falsely negative by the standard ELISA. Dr. Duvic and colleagues found that skin biopsies from HIV-positive individuals gave a positive signal by the PCR assay, whereas those from HIV-negative controls did not. It is expected that the use of PCR will make skin grafting a safer procedure.

An interagency agreement has been established between the NIAMS and the U.S. Army Medical Research and Development Command to study skin manifestations of HIV infection. Under the terms of this agreement, NIAMS staff, directed by Dr. Stephen Heyse, are collaborating with Dr. William James and colleagues at Walter Reed Army Medical Center, Washington, D.C., to carry out clinical, pathologic and epidemiologic studies in HIV-infected Army personnel. It is estimated that at least 400 new HIV-infected Army personnel will be identified annually during the 10-year study.

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DIVISION OF RESEARCH RESOURCES

The General Clinical Research Centers (GCRC) provide a research infrastructure for multidisciplinary studies on both children and adults. Specifically, they provide patient research facilities, computerized data management and analysis, and specialized laboratories for the translation of basic and clinical research into medical practice, as well as research nurses, dietitians, and biostatisticians.

GCRC studies on patients with AIDS and with ARC indicate that the pituitary and adrenal glands are early targets of HIV infection. According to DRR grantee Dr. Edward G. Biglieri and his colleagues at the University of California GCRC at San Francisco General Hospital, damage caused by the virus reduces adrenal steroid production in as many as 30 percent of HIV-infected patients. As the adrenal gland weakens, it becomes a target for opportunistic infections. This often reduces the glands capacity to make cortisol, a steroid essential for the maintenance of life. According to Dr. Biglieri, early HIV infection of the pituitary impairs adrenal gland function, which also lowers the patient's resistance to a variety of diseases. Early detection of adrenal impairment and subsequent treatment with supplemental cortisol during any acute illness can improve the response of HIV-infected patients to treatment.

Ganciclovir has shown promising results in limiting the effects of cytomegalovirus, the major opportunistic virus in AIDS. This virus naturally persists in man; it takes advantage of the progressive destruction of the immune system by HIV to attack the eyes, gastrointestinal tract, lungs, and occasionally the brain. As part of a multicenter study to evaluate the toxicity of a combination of AZT with ganciclovir to slow HIV progression while keeping CMV infections in check, grantee Dr. Douglas Dieterich and associates at the New York University GCRC in New York City studied 18 patients with CMV retinitis, CMV colitis (inflammation of the colon), or other CMV gastrointestinal disturbances. All patients developed toxicity while receiving full doses of both AZT and ganciclovir. When dosage was adjusted down, only about one-third of the patients reacted adversely, and even at the lower dose the combined drugs appeared to be effective. By helping investigators determine the optimum dosages for AZT combined with ganciclovir, this study could lead to a new course of therapy for patients with AIDS and opportunistic infections, allowing physicians to treat both infections simultaneously while avoiding the danger of drug toxicity.

Models of HIV progression developed at the University of Minnesota in Minneapolis by Dr. Lael Gatewood and colleagues use published disease rates to depict the development of

AIDS. A community drug usage model traces the course of AIDS in individuals from recruitment, through increased frequency of use, to outcomes ranging from continued use, recovery, treatment, incarceration, or death. The social network model is based on patterns of needle sharing among friends, strangers, and participants in shooting galleries. According to Dr. Gatewood, these models facilitate the evaluation of risk- reduction strategies, treatment alternatives, and cost-sharing mechanisms. Among the strategies for risk reduction being studied are increased needle sterility, better identification of infected individuals through testing and tracking programs, and reduced addiction through treatment. Dr. Gatewood concludes from her computer simulations that observed differences in AIDS prevalence between communities could reflect random variability rather than fundamental differences in drug usage or risk behavior. The models also suggest that needle sterility programs may be more effective in preventing the spread of AIDS in communities with a low prevalence of infection than in communities where prevalence is high.

DRR's Animal Resources Program (ARP) supports seven Regional Primate Research Centers (RPRC) and their field stations, which provide specialized environments for biomedical research using nonhuman primates. Other programs emphasize the diagnosis and control of diseases of laboratory animals, development of disease models, improvement of animal care facilities, research training programs in laboratory animal medicine, and efforts to develop and implement cell system models, lower organism models, and nonbiological models.

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NATIONAL CENTER FOR NURSING RESEARCH

NCNR-supported research on AIDS focuses on better methods of providing nursing care to patients and families and innovative approaches to educating people about cause, prevention and treatment.

Factors That May Predict High Risk Health Behaviors in Early Adolescence

Dr. Cheryl S. Alexander at the Johns Hopkins University has been following a group of students, beginning in the eighth grade and continuing into high school, to study behaviors that might increase their risk of AIDS or other sexually transmitted diseases, early pregnancy, accidental injuries, and other health problems. Dr. Alexander and her colleagues are looking for differences in personality characteristics and family and peer relationships that distinguish students who frequently engage in health-compromising behaviors from those who do not. They are looking for the effects of these behaviors on school performance, absenteeism, and accidental injuries.

Over 750 students in three rural Maryland counties completed questionnaires in the eighth grade about their overall health, school absenteeism, illness, sexual activity, and behaviors involving risk of injury. They were also asked about ties to religious institutions and the influence of friends on their behavior. In addition, the students completed questionnaires assessing their levels of self-esteem.

In the ninth and tenth grades, students answered the same questionnaires; tenth grade students had additional questions concerning overall knowledge about AIDS and about behaviors that could lead to HIV infection.

In interviews with parents, the investigators gathered information about the children's health habits, health, and physical development, as well as social and psychological adjustment, communications with parents, and family functioning. They also asked about family attitudes toward such subjects as sex, religion and their child's schoolwork. School records were checked to determine school performance and absenteeism. The children were also given physical exams for height, weight, and pubertal development.

Dr. Alexander and her colleagues will be looking at what common personality or environmental factors that may be related to high-risk behaviors and therefore possibly predictive of their occurrence. They will also be determining whether or not engaging frequently in one health-compromising behavior is significantly related to engaging in other health-compromising behaviors.

Developing a further understanding of risk-taking behavior among young rural adolescents can help school nurses, teachers and parents identify teenagers at risk for certain health problems, including AIDS and other sexually transmitted diseases, and can help to develop and implement health education materials and programs to help prevent or treat these problems.

Knowledge About AIDS and Safe Sexual Behavior in Older Adolescents

Sexually-transmitted diseases and drug experimentation, both associated with an increased risk of AIDS, are significant health problems in older adolescents. To develop effective educational programs for this group, more information is needed about their knowledge and attitudes toward AIDS and how such factors affect their sexual behavior.

Dr. Colleen DiIorio at the Center for Nursing Research, School of Nursing at Emory University is administering questionnaires to freshmen in three colleges about the cause, transmission, prevention, and treatment of AIDS. The NCNR grantee and her colleagues are also looking into how these students perceive their risks of acquiring the disease, what they know about safe sexual practices, and why they apply or do not apply their knowledge about these practices.

The investigators will also determine differences in safe sexual practices between males and females and among racial groups. The largest of the colleges (about 1,000 freshmen) is predominantly white and coeducational. The other two are smaller with all-Black populations, one all female and the other all male.

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FOGARTY INTERNATIONAL CENTER

In fiscal year (FY) 1989, the FIC continued development of two AIDS-related international research training programs initiated in FY 1988. Both programs seek to greatly increase the numbers of highly trained epidemiologists, postdoctoral scientists, and clinical investigators worldwide, particularly in developing countries. One program trains foreign scientists from developing countries in epidemiology, while the other provides collaborative postdoctoral research opportunities for U.S. and foreign scientists. Both programs support training in the United States and investigators' home countries. The programs operate through FIC grants to U.S. institutions, which then select participating scientists.

In FY 1989, the FIC added two new institutions to its epidemiology training program, bringing to 10 the total number funded. In the program's first year, these institutions trained 125 investigators from 22 developing countries. Additionally, grantee institutions conducted 25 short-term epidemiological training courses in 12 of these countries.

Examples of research projects implemented through the epidemiology training program are:

- An epidemiological survey of Haitian immigrants living in Miami, where they comprise one of the city's largest immigrant communities. Undertaken by a Haitian participant in the University of Miami program, the survey will be repeated on a larger scale in Haiti.

- An assessment of the neuropsychiatric manifestations of HIV-infected persons in Nairobi, Kenya, particularly among a population of homosexual men. The University of Washington is supporting the work, carried out by a scientist at the University of Nairobi.

- The detection of oral manifestations of HIV-1 infection, including using oral mucosa for clues to of the immune status of AIDS patients. This project is being done by a Harvard program participant from Zaire.

Additionally, the FIC collaborated with NIAID to establish the International Network for AIDS Research and Training. The network links the major international AIDS programs of the NIH, the CDC, the U.S. Agency for International Development, and the World Health Organization. The network prevents duplication of efforts by facilitating the coordination of its participants' activities. It also identifies research and research training needs, and helps organize responses to emerging problems. Two meetings of the network participants were held in FY 1989.

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NATIONAL LIBRARY OF MEDICINE

The National Library of Medicine's collection of some four million items, its MEDLARS® computerized databases, and its Regional Medical Library program are the pillars of a national health information network--a network designed to ensure timely dissemination of scientific and medical information concerning this important disease to the biomedical community.

The Library currently sponsors three AIDS-related online databases on its MEDLARS network: AIDSLINE™, AIDSDRUGS, and AIDSTRIALS (see descriptions below). The Library also publishes the monthly AIDS Bibliography--the latest in a series of AIDS "literature searches" that began in 1983. The Bibliography, with citations of journal articles and books as well as audiovisual materials, covers the spectrum of areas of AIDS concerns--preclinical, clinical, epidemiological, diagnostic, and prevention. It is sold on a subscription basis by the Government Printing Office.

AIDSLINE

AIDSLINE is an online computer file of more than 23,000 references to the published literature on AIDS, dating back to 1980. It is growing at the rate of about 700 new citations a month. AIDSLINE joined NLM's family of MEDLARS databases in 1988, starting as a subset of MEDLINE® (the online equivalent of Index Medicus®). The database was enriched in 1989 with AIDS-related cancer references from NCI's CANCERLIT® file and from another database of references on health planning and administration. Forty percent of the references in AIDSLINE have author-produced abstracts. NLM plans to expand coverage of AIDSLINE, not only with more source journals, but with other forms of information: monographs, audiovisuals, and meeting abstracts.

AIDSDRUGS and AIDSTRIALS

In September 1989, two new databases, AIDSDRUGS and AIDSTRIALS, were added to the MEDLARS system. They provide online access to current information on clinical trials of AIDS drugs and vaccines, including the general criteria for patient participation in those trials. Part of the PHS response to Public Law 100-607, or the HOPE legislation, the two databases are made up of information provided to NLM through the FDA and NIAID. The FDA provides information on privately sponsored experimental tests of efficacy, and NIAID provides information about NIH-funded safety and efficacy trials.

AIDSTRIALS contains information about clinical trials of agents undergoing evaluation for use against AIDS, ARC, and

AIDS-related opportunistic diseases. The information in the database includes the title of the trial, the trial purpose, the agent(s) being studied, the trial phase, diseases studied, patient inclusion and exclusion criteria, locations at which the study is taking place, and whether the trial is still adding patients. Details about the medication regimen may also be included. Each record contains the telephone number of a contact person able to provide additional information.

The companion database, AIDSDRUGS, contains descriptive information about the agents being tested in the clinical trials. Agent descriptions include standard chemical name and synonyms, pharmacology, contraindications, adverse reactions, manufacturer, and certain physical/chemical properties.

PHS currently also makes this information available through NIAID's toll-free, confidential telephone service (1-800-TRIALS-A), as required by the HOPE legislation. Having the databases available on NLM's system, however, gives those with a repeated need for such information--physicians and community-based AIDS organizations, for example--the option of performing their own searches directly, online.

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OFFICE OF THE DIRECTOR

The Office of the Director, NIH, continues to support, through its Office of AIDS Research (OAR), the AIDS Program Advisory Committee, which was established to advise the Director on priorities for AIDS research at NIH. With its membership drawn from the country's most distinguished scientists, public administrators, and ethicists, the Committee has met to discuss developments in therapeutics, vaccines, and access to clinical trials for underserved populations.

The OAR coordinates the NIH AIDS program, assisting the Director in the development of NIH-wide policy related to AIDS research. Through the NIH AIDS Executive Committee, composed of the Directors and AIDS Coordinators of the NIH Institutes, OAR coordinates the NIH AIDS research plan, addressing the scientific, legislative, economic, and public policy matters relevant to that research.

Through OAR, work also continues on the development of a central NIH database on AIDS research that will include information on laboratory research as well as AIDS clinical trials. When complete, this database will provide an online, continuously updated source of administrative information on all AIDS projects supported by NIH.

FUTURE DIRECTIONS

Research related to the acquired immunodeficiency syndrome is expected to expand in a number of different directions, including clinical manifestations, pathogenesis, therapeutics, vaccine development, and neuroscience. As the nature of AIDS changes, from an acute illness to a chronic disease, emphasis is shifting to early detection of HIV seropositivity so as to implement appropriate therapeutic interventions.

The development of better diagnostics will improve the quality of patient care and provide information essential to the study of the natural history of AIDS. The continuing evolution of technologies such as PCR and monoclonal antibody production will facilitate earlier treatments for HIV infection and PCP. In addition, further development of these techniques will enable physicians to more accurately diagnose HIV infection in the newborn.

In basic research, cellular, molecular, and chemical studies of HIV will continue to expand our the understanding of the mechanisms of infection, viral activation, and immune system suppression. The further elucidation of the regulation of HIV genes will aid scientists in their search for the key to blocking the viral life cycle in infected individuals.

Drug development will maintain its high priority in AIDS research as scientists continue to screen large numbers of compounds in the laboratory and to use the sophisticated techniques of structural biology to design targeted anti-HIV agents. The modification of existing compounds provides another promising avenue in the development of therapeutics, as do the combination and optimization of current therapies.

In the area of clinical trials, earlier trials are being expanded to provide more information on new therapies, and to broaden early access to these drugs. Special efforts will be continued to include more minorities, women, and children in clinical trials.

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FOOD AND DRUG ADMINISTRATION

ACQUIRED IMMUNE DEFICIENCY SYNDROME

The conquest of AIDS has been identified by former President Reagan and President Bush as the nation's number one public health priority. The disease has reached epidemic proportions. Since it was first reported in 1981, over 113,000 persons in the United States have contracted AIDS, and more than half of these persons have died.

As the largest consumer protection agency of the Federal Government, FDA plays a major role in the Federal Government's response to the AIDS epidemic. FDA is responsible for assuring the safety and effectiveness of drugs, biologics, and medical devices and has responsibility for safeguarding the nation's blood supply. Clinical testing of AIDS therapies must be approved by FDA, and it is FDA's responsibility to determine whether those AIDS therapies are safe and effective for marketing in the U.S. FDA is exerting tremendous effort to expedite the development, review, and approval of promising therapies and, where appropriate, facilitate expanded access to promising investigational therapies to persons for whom no alternative therapies are available.

Research Activities

A strong program of scientific research is essential to maintain the quality and timeliness of FDA's review of AIDS products. Up-to-date expertise leads to authoritative product evaluation. Expertise in such areas as pharmacokinetics can aid manufacturers in designing trials that can streamline product approval. To enhance FDA's regulatory ability, a research program in cytokine biology has been established within FDA to study the basic immunologic defects associated with AIDS and to discover means to ameliorate these defects.

FDA is continuing its collaborative studies with the National Institute of Allergy and Infectious Diseases (NIAID) and the National Cancer Institute (NCI) in characterizing the immune responses, monitoring viral infection, and studying antiviral and immunotherapeutic drugs in AIDS patients. In addition, FDA has established collaborative efforts with other agencies in the accomplishment of these and other goals related to the treatment and prevention of AIDS and HIV infection.

Included in the research FDA conducts are studies on: (a) the adequacy of the processes used to prepare anti-hemophiliac factor (Factor VIII) and immunoglobulin in the inactivation of HIV; (b) the effects of antiviral compounds on replication of HIV; (c) the molecular biology of HIV; (d) primates to develop an animal model for AIDS; (e) the epidemiology and immunology of HIV infections as they relate to the safety and effectiveness of regulated products; (f) the significance of HIV infections with respect to safety of

biologic products; and (g) the etiology and pathogenesis of Kaposi's Sarcoma. Also, FDA licenses and monitors the HIV antibody test kits, and evaluates the safety of blood products. FDA is, in addition, funding studies to determine the safety and efficacy of AIDS vaccines, as well as the efficacy of blood donor criteria, and the testing for HIV antibodies and antigen in blood donors.

In order to focus attention on issues concerning blood screening and the safety of injected blood products, FDA has created a new laboratory of retrovirology. Among other things, the laboratory is engaged in research on detection of HIV infection by culture, gene amplification, and inactivation of virus in the manufacture of blood products. In addition, FDA has created a new Division of Cytokine Biology in response to the growth in recombinant products dealing with AIDS and AIDS-related diseases. FDA has also completed the construction of special laboratories to permit safe use of live HIV in some experiments.

New Drug Evaluation

It is FDA's responsibility to approve safe and effective drugs used in the care and treatment of AIDS patients. Special emphasis is being placed on producing the most timely and efficient premarketing review possible of drug products which offer promise for diagnosing, treating, or preventing AIDS and AIDS-related diseases.

FDA's strong commitment was demonstrated initially by the timely and thorough premarket review of the drug Retrovir, (Zidovudine, formerly known as AZT), the first drug approved for use in AIDS in March 1987. Retrovir was the first drug to go completely through the 1-AA designation process which was created in June 1986 as an extension of the existing classification system for review of New Drug Applications (NDAs). This designation was established to assure that all potential AIDS therapies would receive the highest priority in the drug review process. The expedited drug approval process has also resulted in the licensure of human interferon Alpha 2 for the treatment of AIDs-related Kaposi's Sarcoma, aerosol pentamidine for prevention of pneumocystis pneumonia, and ganciclovir for use in treating viral retinal infections among persons with AIDS.

As of November 1, 1989, FDA has received over 300 Investigational New Drug Applications (INDs) for approval to test new AIDS drugs, biologics, and vaccines in humans. Over 250 INDs remain active including 56 antiviral drug INDs, 63 immunomodulator INDs, nine vaccines, five anti-neoplastics, 56 INDs for drugs for opportunistic infections, 47 diagnostics, and 20 hematologic-related factors. The number of applications for new investigational AIDS therapies reviewed by FDA has averaged about six per month in 1989.

Six Treatment INDs have been approved since the Treatment IND regulations became effective in June 1987. Four remain active,

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the other two, for aerosol pentamidine and ganciclovir, terminated upon product approval in June 1989.

In addition, ddI, a new antiretroviral drug, has been made more widely available both under a Treatment IND and through an open safety protocol in parallel with the phase II controlled clinical trials, a new approach to combining the drug development process with wider treatment availability.

FDA's other special initiatives in the area of new investigational AIDS therapies include improvements in management such as: plans for development of an on-line computerized tracking system for all AIDS review activities, including INDs, NDAs, PMAs (Pre Marketing Applications), and other drug/biologic applications; development of the FDA component of the National AIDS Clinical Trials Information Service, a database providing public access to information about AIDS-related clinical trials; creation of the Division of Antiviral Drug Products; creation of the AIDS Coordination Staff to promote intra-and inter-agency cooperation on crosscutting issues; establishment of a special team approach to provide selected pharmacokinetic data and guidance as needed to sponsors; and a series of workshops with the Institute of Medicine and others on clinical trial design for premarket evaluation of AIDS-related products. In addition, FDA is working closely with the National AIDS Program Office, the National Institutes of Health, other governmental and private organizations and concerned individuals to develop a "parallel track" policy whereby promising new investigational therapies can be made available to persons with AIDS and HIV infection who cannot participate in controlled clinical trials.

HIV Detection

Progress continues on the development of satisfactory test methodologies for HIV antibody detection. To date, there are ten licensed manufacturers of HIV antibody test kits including ELISA screening tests, one particle-agglutination screening test, and one Western Blot test. Currently, there are more than 15 pending applications for new kits or amendments for refining existing ones. In August 1989, FDA licensed the first diagnostic kit to detect the presence of HIV by directly detecting the proteins, or antigens, of the virus. This new HIV-1 antigen test is approved to help physicians diagnose and follow the medical status of HIV-infected persons. It is not intended for use in screening blood or plasma donations.

Among the new product applications are several forms of testing which need to be validated for clinical use. These include:

1. Additional tests to detect circulating viral antigen during various phases of HIV infection with potential clinical applications.

2. Antibody screening test using viral antigens produced by gene cloning or peptide synthesis. Such recombinant peptide-based tests may offer improvements in the sensitivity and specificity of antibody detection and may also facilitate tne development of rapid and inexpensive tests for widespread use. In addition, the use of recombinant peptides may greatly reduce the risks posed to laboratory workers involved in the manufacture of antibody test kits.

3. Several new product applications have been received for Western Blot and immunofluorescence tests.

4. Screening assays designed to detect antibodies to other retroviruses (i.e., HIV-2). Regulation of these products has raised issues similar to those handled by FDA in relation to the regulation of the first HIV screening tests such as the development of reference reagents and criteria for measuring sensitivity and specificity.

5. Test kit manufacturers have submitted amendments for the use of dried blood spots as a sample source for HIV antibody testing. Such procedures would facilitate public screening. Review of FDA policy concerning such test kits is under way.

In November 1989, FDA published in the Federal Register a notice to all manufacturers of in vitro tests for HIV antibody, and other interested parties "points to consider" in the manufacture and clinical evaluation of such test kits. This notice addresses the non-regulatory questions most frequently asked concerning the evaluation and approval of HIV antibody test kits and is intended to facilitate communication between the Agency and individuals interested in making applications to FDA.

HIV antibody testing, continuing in all blood banks, donor centers and plasmapheresis centers, has been augmented by the licensed Western Blot test which serves as the basis for reentry of blood donors tentatively deferred because of nonrepeatable, false-positive results from initial screening. Use of the Western Blot has remarkably upgraded the specificity of information derived from donor screening. Also, use of this test in a reentry algorithm has permitted approximately 80 percent of deferred donors to be reinstated without compromising blood safety.

Universal HIV testing of donated blood and blood products has reduced the rate of confirmed positive antibody tests in donors. This change may be due to several factors which include permanent exclusion from the donor pool of individuals with detectable

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antibodies as well as successful implementation of education and self deferral programs in blood and plasma centers. A reduction in the rate of HIV antibody positive donors implies increased safety of blood and blood products available for use in the U.S.

FDA revised the package insert labeling of HIV antibody test kits to permit a claim for clinical diagnostic use. This has made testing more widely available for purposes other than blood screening. Consideration is also being given to developing testing programs, home sample collection, mail-order testing, and notification. While such programs would offer the public wide access to HIV tests at a high level of confidentiality, significant problems are posed for effective regulation of the testing and assurance of adequate counseling following a positive test result. FDA has published a proposed rule which would restrict such mail-order testing to collections obtained in a comprehensive health care facility, has held a public hearing on the proposed rule, and is reviewing public comment now.

FDA recently approved licensure of antibody screening tests for another human retrovirus, HTLV-1, which is not associated with AIDS, but which causes a rare leukemia and a neurological disorder. The FDA has recommended screening of blood intended for transfusion since studies in the U.S. have confirmed a significant prevalence of infection by this virus in blood donors, and it is known that certain blood components can transmit the virus to recipients. FDA is continuing its involvement in surveillance testing of U.S. populations to identify the possible introduction of a new class of AIDS-causing retroviruses, called HIV-2, which has already been detected in some countries in Western Europe.

Progress continues in the development of improved methods of virus inactivation in antihemophilic factor preparations. In particular, liquid pasteurization in the presence of protein stabilizers and treatment with detergents and organic solvents seem to offer significant benefits. The use of monoclonal antibody columns offers an additional method of improving virus clearance while also increasing the specific activity of the materials. Products have been licensed which use these technologies, and an effort is ongoing to upgrade the industry standards for acceptable inactivation of virus in these products.

In addition to assisting in the organization of workshops dealing with the proper use and interpretation of antibody tests, FDA also sponsored a large scale study on the effectiveness of HIV antigen testing as a screen for donated blood or plasma. The study involved over 500,000 donors and indicated no improved safety by the addition of the antigen test kit to the current screening procedures for blood and blood products. Similar efforts have been undertaken to define the role of HTLV-1 antibody testing in blood bank screening. FDA has developed contracts for the management of large serum repositories which can be used to validate the sensitivity of commercial tests for HIV and HTLV-1 antibodies. FDA supports the World Health Organization in its efforts to develop

international guidelines for HIV test evaluation and standardization particularly in the area of interpretation of Western Blot and other tests used to confirm antibody screening tests.

HIV Transmission - Blood

As noted previously, protection of the nation's blood supply is an ongoing FDA regulatory responsibility which has become vital in the context of the AIDS epidemic. Although the risk of acquiring human immunodeficiency virus by transfusion of blood has almost been eliminated with blood and donor screening efforts, FDA expanded its inspections of blood collection facilities to ensure the presence of effective quality controls and to ensure compliance with requirements for HIV testing. In 1988, FDA increased its inspections of all such FDA regulated facilities in the U.S. from biannually to annually. Although these inspections revealed slight deviations in procedures from FDA regulations, no confirmed HIV antibody positive (HIV contaminated) units had been transfused. Regardless of this, FDA plans to continue this expanded effort in order to ensure that the safety of the blood supply is sustained and continues to promote the use of autologous, instead of homologous, blood for elective procedures that may require transfusion.

Due to a number of reported cases of HIV transmission, much attention has been given recently to the problems of insuring the safety of health workers and laboratory workers involved in the handling and processing of blood. In particular, consideration is being given to the adoption of universal blood precautions and to the strict adherence to published biosafety guidelines for sample handling and processing. FDA continues to work with the Centers for Disease Control and other agencies in efforts to define improved ways to reduce the risk of exposure to HIV through the handling of blood and blood products.

HIV Transmission - Medical Devices

In its ongoing responsibility to assure the safety and effectiveness of medical devices, FDA has launched a program that concentrates on preventing the transmission of AIDS and AIDS-related diseases through such barrier products as condoms and surgical gloves and commonly-used clinical devices such as dental drills. FDA is surveying the methods of disinfection of clinical devices to learn how sterilization procedures may be improved and is working with device manufacturers to improve device design in ways that minimize risk.

In the field, FDA is inspecting manufacturers and processors of both domestic and foreign-made condoms to ensure conformance with FDA's criteria for acceptability. Since implementation of this program, FDA has tested over 180,000 condoms from about 700 batches of condoms. Batches with more than four defects per 1000 condoms were not permitted to reach the U.S. market. These efforts are

leading to increased quality control by manufacturers. In 1988, FDA increased its surveillance of surgical and examination gloves, testing over 26,000 individual gloves on the market. Failure rates were found to be high, particularly in shipments of imported gloves, and FDA developed a more stringent and sensitive method to test glove integrity in order to improve the quality of medical gloves. In November 1989, FDA published a Federal Register Notice to establish a sampling and testing program for the examination of surgical gloves. In addition to these ongoing inspection efforts, FDA is continuing research into improvement of barrier effectiveness, as well as efforts to expedite the review of an increasing number of applications for approval of these products.

Vaccines

FDA has studied the immunology of AIDS and demonstrated that some proteins of HIV are targets for human immune responses and could be used in developing a vaccine against the virus. A rapid and sensitive microneutralization assay has been developed and is being used to evaluate the specificity of immune responses induced by candidate vaccines. Studies are continuing to develop information necessary for evaluation of vaccine safety and efficacy. FDA has begun developing potency tests for candidate AIDS vaccines. In addition, studies to characterize four cellular immune responses to HIV antigens are in progress. Cell-mediated responses may come to play an important role in vaccine-induced disease prevention.

FDA is defining issues that should be addressed prior to initiation of Phase I vaccine clinical trials and in anticipation of efficacy studies. FDA has frequent joint meetings with manufacturers of candidate vaccines. Manufacturers are encouraged to request such meetings as early and as frequently as needed. These meetings assure the exchange of information that will facilitate preclinical and clinical development and IND review. FDA continues its policy of reviewing AIDS-related IND applications for vaccines as quickly as possible. To date, nine IND applications for AIDS vaccine have been received, and several have been approved for Phase I clinical studies.

Extramural studies related to evaluation of the safety and efficacy of AIDS vaccines are being conducted worldwide. Collaborative studies with investigators in the U.S., Europe, the Caribbean, Africa, and South American have begun to look into immune responses to HIV infection. Information derived from these studies will be directly applicable to AIDS vaccine development.

Other Areas of Activity

The Agency is compiling a compendium of information on nutritional needs of persons with AIDS as part of an effort to improve the health quality of those affected by HIV.

A video on food safety, recently developed and released by FDA and the Centers for Disease Control and aimed at preventing transmission of foodborne illness among persons with AIDS and HIV infection, has been well received by the public.

FDA is also developing a brochure which provides the same food consumption and handling advice for persons with AIDS and will distribute it through the National AIDS Information Clearinghouse.

FDA has developed state contracts to establish AIDS Health Fraud Task Forces in 17 states, District of Columbia, and Puerto Rico. These task forces will include the FDA district AIDS coordinators, state AIDS coordinators, community-based organizations, health care professionals, state and local health agencies, state attorneys general offices, United States postal inspectors offices, and consumer groups. These task forces will ensure that information concerning AIDS fraud is distributed quickly and that necessary action to prevent AIDS health fraud can be taken.

FDA has developed a booklet to educate condom users regarding prevention of HIV and other sexually transmitted diseases. This brochure has been prepared with consultation and encouragement from 12 governmental components and 8 national health professional organizations. The Agency has also developed an educational project for patients and health professionals concerning renal dialysis and AIDS as well as a program in conjunction with other health agencies to educate dental professionals about AIDS and infection control.

FDA communicates with health professional organizations, community-based research groups, individual physicians, as well as selected international organizations and foreign regulatory authorities on such topics as Treatment INDs, investigational products, and newly marketed FDA-regulated products for the diagnosis, treatment and prevention of HIV infection, AIDS, and AIDS-related conditions.

In support of its interest in and commitment to community-based research, the Agency works with public and professional organizations to encourage useful and effective research studies to support AIDS-related product approval. FDA has sponsored workshops to provide community physicians and other community-based researchers with the information and technical assistance necessary to meet FDA requirements for conducting clinical trials. FDA staff have also participated in similar workshops sponsored by other agencies and private organizations. FDA is also working closely with the Community Clinical Research Program in the NIAID's AIDS Program to coordinate activities and provide assistance in training their contract grantees.

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CENTERS FOR DISEASE CONTROL

Human Immunodeficiency Virus (HIV)/Acquired Immunodeficiency Syndrome (AIDS)

HIV infection continues to be the number one public health problem in the United States. As of November 30, 1989, a cumulative total of 115,158 of AIDS cases had been reported to CDC, including 1,947 cases less than 13 years of age. Over half of the reported cases have died. Of the 1,947 children reported, 530 cases, or 34 percent, were reported during the past year. As of November 30, 1989, 32,603 cases were reported during calendar year 1989. Racial and ethnic minority populations continue to be disproportionately affected by the new epidemic. Blacks and Hispanics account for 26.9 percent and 15.4 percent, respectively, of the reported cumulative adult AIDS cases. Blacks represent 53 percent, and Hispanics 24.5 percent of the pediatric cases.

In fiscal year 1990, CDC will conduct activities to further clarify the epidemiology and natural history of HIV infection through surveillance of AIDS cases, seroprevalence surveys and studies of HIV infection, epidemiologic studies, and laboratory investigations. In addition, CDC will intensify prevention strategies and increase the transfer of technology designed to prevent and control the transmission of HIV. CDC will conduct and/or support activities including:

- o National surveillance of AIDS cases;
- o Pilot studies of HIV surveillance through State and local health departments;
- o Domestic and international epidemiologic studies to identify risk factors and further define and quantify co-factors and modes of transmission; development and evaluation of prevention strategies;
- o investigation and evaluation of new serologic and other diagnostic tests;
- o research on an improved animal model for HIV infection;
- o collaborative vaccine development and evaluation;
- o transfer of technology to the medical and public health communities to facilitate early intervention in HIV infection.

CDC will continue to provide HIV prevention information and education to individuals, health care workers, high-risk groups, scientific and public health communities, and the public in support of the overall goal of preventing HIV infection. Cooperative agreements will continue with State and local health departments to conduct active HIV/AIDS surveillance. Cooperative agreements will support 450 sentinel surveillance projects to determine seroprevalence of HIV infection through State and local health departments, other public facilities, and selected private institutions covered by the Family of Surveys.

SURVEILLANCE

CDC will monitor, analyze, and project national trends for HIV infection and AIDS incidence by geographic area and groups at increased risk. Among other purposes, active surveillance will help clarify risk factors, patterns of transmission, and provide data used in the formulation of prevention strategies, public policy, and the allocation of resources at all levels to combat the epidemic.

EPIDEMIOLOGIC STUDIES

Since 1981, CDC has conducted specialized, intensive epidemiologic studies to: contribute to understanding the natural history of HIV; investigate modes of HIV transmission; identify those at risk; document co-factors associated with increased risk for acquiring the infection; and provide HIV risk-reduction guidelines and prevention recommendations applicable to large segments of society. CDC-sponsored investigations include studies of homosexual and bisexual men, intravenous drug users, persons with hemophilia, transfusion-associated AIDS cases, sexual partners of persons with HIV infection or at increased risk for the disease, children with AIDS, newborns with HIV infection and AIDS-infected women of childbearing age, infected pregnant women, heterosexual transmission and female prostitutes.

To further define risk factors for HIV transmission and to clarify the natural history of infection, CDC will initiate, continue, or expand, studies of: pregnancy outcomes, newborns acquiring the virus from their mothers; families of children with transfusion-associated HIV infection; increased deaths among intravenous drug abusers from respiratory conditions thought to be associated with HIV infection, AIDS patients reported with undetermined risks; heterosexually-transmitted HIV infection; transfusion-associated HIV infection; risk factors for transmission among a cohort of homosexual men in San Francisco; sex partners of homosexual men; family members of persons with AIDS and HIV-related infections to further examine transmission factors; donors of blood to persons who develop transfusion-associated HIV infection; recipients of blood and organ transplants from donors later found to be HIV-infected; transmission in prisons; infection in female prostitutes; patients with lymphadenopathy syndrome (LAS) to determine any changes in risk factors for developing AIDS; neurologic aspects of HIV infection; surveillance and epidemiologic investigations of persons infected with HIV-2, (19) HIV-1 and HIV-2 transmission in Africa; investigations of HIV transmission factors in Thailand; and risks of HIV infection in aerosols generated by surgical/operative procedures.

LABORATORY INVESTIGATIONS

CDC will continue laboratory investigations of HIV to: provide viral isolation, serologic and immunologic support for epidemiologic and seroprevalence surveys and studies; assess sensitivity and specificity of serologic tests; develop and evaluate new screening (polymerase chain reaction) and diagnostic tests; assess differences among virus isolates from various geographic areas for possible variability in patterns of host response and pathogenicity; determine whether detection of virus protein and/or nucleic acid sequences are useful in rapid diagnosis of infection; correlate clinical and epidemiological findings with antibody to HIV and positive cultures of this virus; determine immunologic responses to infection with HIV; document the susceptibility of HIV to disinfectants and sterilizing procedures; clarify the natural history of infections in primates and other animals infected with HIV; accelerate the development of therapeutic technologies through animal model investigations; and participate in vaccine development and evaluation.

Resources will be focused upon improving screening and diagnostic technologies to identify persons earlier in the course of their infection. This effort will improve the safety of the world's blood supply, enhance clinical care through early intervention, and improve HIV prevention and control outcomes.

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NATIONAL LABORATORY EVALUATION PROGRAM

A National Laboratory Evaluation Program has been developed to assess the capability of the Nation's laboratories in performing currently available tests used in prevention and control of HIV infections and AIDS. Currently, there are over 1,400 laboratories enrolled in this voluntary program.

Performance evaluation samples have been shipped to the participants periodically and results are being analyzed. Additional evaluation and improvement activities planned include: identification and characterization of HIV testing laboratories; shipment and analysis of performance evaluation serum panels; correlation of characteristics with laboratory performance; development of methods of estimating sources of error in the entire testing process; and implementation of intervention strategies.

CDC continues to develop and modify prevention recommendations for individuals at increased risk of infection, health-care workers, and the public. PHS prevention recommendations to reduce the risk of HIV transmission were first issued in November 1982, for clinical, laboratory, and animal research workers and in March 1983, for blood donors, members of risk groups, and sexual partners. A total of 48 major guidelines related to prevention of AIDS and HIV transmission have been developed and distributed, with six published in 1989. Future guidelines will be based on ongoing epidemiologic research intended to clarify and quantify the risk of HIV groups and to identify specific behaviors, factors, or co-factors which increase susceptibility. Dissemination of information and recommendations is facilitated by CDC's continued financial and technical assistance for an information interchange system among city governments through the U.S. Conference of Mayors. The interchange system will make timely and appropriate information about HIV infection available to mayors and local health officials, especially in heavily affected cities.

CONTROL STRATEGIES

The strategy to control the spread of HIV is influenced by five crucial facts: (1) no effective therapies exist to eliminate virus from an Infected Person; (2) no vaccine exists to prevent susceptible persons from acquiring HIV infection; (3) infected individuals may transmit the virus throughout their lifetime; (4) spread of the virus results from a limited number of personal behaviors, which, when altered, can reduce or prevent transmission of the virus; and (5) HIV infection represents the first contemporary infectious disease causing significant morbidity and mortality for which public health prevention and control measures and individual behavior change remain the major intervention tools. Related control mechanisms include: (1) expansion of drug abuse treatment capacity; (2) expansion of STD control programs; (3) provision of contraceptive information to infected women who are identified through HIV counseling and testing programs; (4) continued testing to insure a safe blood supply; and (5) increased vigilance regarding the self-deferral of prospective at-risk blood donors.

The goal of the control strategy, therefore, is to reduce HIV transmission by influencing the behavior of people in three specific population groups. The primary effort is to apply individually-targeted health education messages to persons who are already infected so they will adopt behaviors that reduce

their risk of infecting others. The second is to deliver risk reduction messages that will help prevent infection in people who are uninfected, but whose current personal behaviors place them at high risk of acquiring an infection. The third is to reach the general public with timely and accurate information that defuses unjustified fears, facilitates rational behavior toward all aspects of the HIV epidemic and promotes constructive support for public health control efforts. Preventing the spread of HIV requires the successful implementation of two major strategies. The first strategy attempts to discourage persons from adopting risky behaviors by promoting health behaviors through group level interactions, such as school health settings. The second strategy attempts to reach individuals at high risk at the personal level, helping them to better understand their vulnerability to infection, promoting less risky behavior and alternate safe behaviors, and helping them gain the skills and support to maintain a low-risk lifestyle.

The focus of program services at the personal level is to provide both high risk individuals, and their partners, with education tailored to their unique situations and particular needs for assistance.

In fiscal year 1987, the AIDS Health Education/Risk Reduction (HE/RR) and Counseling and Testing Site (CTS) cooperative agreements were consolidated as the primary components of the HIV Prevention Program. Further consolidation occurred in fiscal year 1988 with the addition of surveillance activities, including a seroprevalence component, that were previously funded as a separate program.

In addition to HE/RR and CTS, the prevention component includes a minority initiative and public information campaign component. Agreements are in place with 50 States, the District of Columbia, eight territories and five municipalities.

Since health education is the primary strategy for controlling transmission of HIV, it is essential to identify the most effective methods of applying these techniques to test them and other evolving control measures under actual program conditions, and to disseminate information to all States. To these ends, CDC has awarded seven cooperative agreements supporting on-going community-based demonstration projects for HIV prevention and risk reduction. The findings of these projects are routinely evaluated and disseminated to the prevention projects.

RACIAL AND ETHNIC MINORITY POPULATIONS

Because AIDS affects racial and ethnic minority populations disportionately, CDC will continue to provide to State and local health departments funds which are specifically targeted to this important group. In 1989, support was also provided to 32 national and regional minority organizations. In addition, funds are being provided to the United States Conference of Mayors to support HIV information exchange and to expand funding to 23 minority-oriented, community-based organizations (CBOs) committed to HIV information programs. In 1989, funds for HIV information and education were also awarded directly to local minority CBOs in 27 metropolitan areas having the highest cumulative number of reported AIDS cases among racial and ethnic minority populations. Funding and technical assistance will be continued in 1990 to these CBOs.

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NATIONAL PARTNERSHIP PROGRAMS

Persons with hemophilia are a special group at high risk for HIV infection and AIDS. Consistent with Congressional intent, CDC provides funding through an interagency agreement with the Human Resources Services Administration (HRSA) for a national HIV educational effort directed to persons with hemophilia and their sex partners. CDC collaborates with the National Hemophilia Foundation and HRSA in conducting these activities through the national network of Comprehensive Hemophilia Treatment Centers. This major initiative will continue in fiscal year 1990. Collaboration between CDC and the American Red Cross (ARC) continued in 1989 through the existing cooperative agreement between these organizations. CDC provided ARC with $6.3 million dollars to continue development of a core curriculum of AIDS prevention information for use by ARC's 2853 chapters throughout the United States. This curriculum includes education modules directed respectively to black and Hispanic youth and their families and for educational efforts in workplace settings. In FY 1989, over 38 million brochures were distributed free by the ARC and over 1.5 million persons attended 19,600 ARC presentations on HIV and AIDS prevention.

SCHOOL HEALTH EDUCATION:

CDC continues to support a program, School Health Education to Prevent the Spread of HIV Infection, designed to help school personnel and others plan, implement and evaluate effective education about AIDS and HIV infection for youth. The schools are a particularly important focus for HIV prevention efforts as more than 45 million young people are currently enrolled in some 100,000 elementary and secondary schools across the country and more than 12 million additional students are enrolled in colleges and universities. The program will enable schools, and organizations serving youth not in school, to identify and develop effective AIDS educational strategies that are consistent with community values and needs.

CDC has established cooperative agreements with 20 national organizations to increase the number of schools, and agencies serving youth not in school, that provide effective education about AIDS. The national organizations target black and/or Hispanic youth, incarcerated youth, runaway youth, and college and university populations.

Cooperative agreements have also been established with 71 State, territorial and local education agencies in jurisdictions with the highest cumulative number of reported AIDS cases to provide locally-determined education for school-aged populations. Two State and one local education agency received additional funding to establish training/demonstration centers. These centers provide training to State and local education agency representatives from across the country on how to implement effective HIV education in their school systems.

The AIDS School Health Education Subfile, part of the Combined Health Information Database, became operational in 1987. As of November 1989, the annotated bibliography of the AIDS Subfile contained over 400 abstracts of curricula, policies, teaching materials, and programs related to AIDS and HIV. The subfile provides educators across the Nation with ready access to a wide variety of materials developed at the national, State and local levels

NATIONAL PUBLIC INFORMATION PROGRAM

To reach the general public, in fiscal year 1987 CDC initiated a national information campaign with the theme, "America Responds to AIDS." The campaign was designed to: (1) provide national significance and visibility to actions that will prevent HIV infection; (2) reach both the general population and special targeted groups; and (3) develop strategies that will be used in the future. In 1988, as a part of that campaign, CDC developed a brochure on the prevention and control of HIV infection entitled "Understanding AIDS." The brochure was mailed to 107 million households in the United States. In the fall of 1988, a campaign phase targeted to "Women at Risk" and "Sexually Active Adults with Multiple Partners" was disseminated.

In May 1989, the "Parents and Youth" phase of the campaign directed to parents and other concerned adults who work with youth was released. A guide for use by parents and other adults was developed in cooperation with representatives from many agencies serving youth. The guide was publicized through English and Spanish television, radio, and print public service announcements which listed the National AIDS Hotline as the request resource; over 650,000 copies have been mailed from the Clearinghouse in response to this campaign. Implementation of the program has been accomplished through numerous organizations including: the National Parents and Teachers Association (PTA); the American College Health Association; the National Education Association; State health and education agencies; and religious organizations through their publications.

In fiscal year 1989, CDC initiated a study to determine the feasibility of purchasing media time and space as an option for reaching selected populations.

The National AIDS Information Clearinghouse System was initiated in fiscal year 1987 to respond to the needs of officials and program managers at all levels for resources and materials which may be used in program development as well as to meet the information needs of the general public. Two databases (one of organizations involved in HIV and one of materials) were subsequently developed and added. Reference specialists at the Clearinghouse use these resources to respond to both telephone and written inquiries. Direct access to the databases has been provided to officials and managers who have computer systems, and beginning in January 1989 access to the materials database service was provided through the Combined Health Information Database. New database elements are being developed as needed to provide answers to other inquiries such as sources of funding. Over one million items of HIV informational materials continue to be mailed from the Clearinghouse each week in response to inquiries.

In 1989, the National Institute of Allergy and Infectious Diseases (NIAID), the National Library of Medicine (NLM), and the Food and Drug Administration (FDA), inaugurated a database of clinical trials and drug protocols information for the public through a toll-free hotline (1-800-TRIALS-A) managed by CDC's National AIDS Information Clearinghouse. Five to six hundred calls are being received each week.

In fiscal year 1990, CDC's existing contracts for the National Public Information Campaign and the Clearinghouse will expire. Applications for new contracts will be solicited on a competitive basis.

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The National AIDS Hotline has been greatly expanded to respond to growing public information needs. The Hotline toll-free system (1-800-342-AIDS) was connected to the Clearinghouse database in fiscal year 1988 to expand the scope and validity of the information used. An Hispanic Hotline (1-800-344-SIDA) was established in May 1988, and the Telecommunications Device for the Deaf (TDD) service was initiated in August 1988. The number of calls annually to the Hotline is approaching 2 million.

Awards were made to 10 national organizations to initiate prevention programs to reach general populations. These included grants to three unions and the National Conference of State Legislators.

PROGRAM ACCOMPLISHMENTS FOR 1989

The following are highlights of achievements in fiscal year 1989:

A. Epidemiology and Surveillance

1. Conducted epidemiologic studies and analyses of HIV infection in long-term survivors of HIV infection, homosexual men, healthy males with lymphadenopathy, intravenous drug abusers, persons with hemophilia, dialysis patients, transfusion-associated AIDS cases, pediatric AIDS, sexual partners of persons with AIDS or at increased risk for infection, health-care workers, and studies to examine the risk factors for transmission associated with heterosexuals and female prostitutes.

2. Collaborated with the Government of Zaire, the National Institute of Allergy and Infectious Diseases (NIAID), and the Institute of Tropical Medicine (Belgium), to conduct active AIDS surveillance, epidemiologic studies, and laboratory investigations in support of Project SIDA HIV-related projects.

3. Funded 65 Cooperative Agreements with State and local health departments, the District of Columbia, the Commonwealth of Puerto Rico, and U. S. Trust Territories to support active surveillance of AIDS cases.

4. Managed a contract for mathematical and computer simulation models to describe both the transmission and spread of HIV infection and the incidence of AIDS associated with routes of transmission.

   Models will be used to assist in projecting the number of infected individuals and AIDS cases through 1993 by transmission category, age group, gender, and race/ethnic group.

5. Implemented a national HIV seroprevalence Family of Surveys plan through State and local health departments and additional organizations to reach selected U.S. populations including: military recruits, American Red Cross blood donors, STD clinic patients, IV drug abusers, family planning clinic patients, childbearing women, Job Corps applicants, prisoners, migrant workers, college students, and other populations.

6. Produced and distributed a cumulative monthly surveillance summary of AIDS cases reported to CDC.

7. Increased the number of studies of pediatric AIDS cases and transmission, including expanded perinatal transmission studies and development of a comprehensive pediatric AIDS case report form.

8. Expanded sentinel hospital-based surveillance to 40 hospitals to determine prevalence and trends of HIV infection in patients.

B. Laboratory Studies and Support

1. Continued studies with a DNA amplification technique, the polymerase chain reaction, to rapidly detect HIV genetic sequences in chromosomal DNA.

2. Continued initial studies on new human herpes virus (HIV6) from cells of AIDS patients.

3. Continued laboratory surveillance for the introduction of new HIV variants into the U.S. Intensified work continues to document the presence of HIV-2 infections in the U.S.

4. Continued studies to increase understanding of the duration of HIV infection before the detection of antibody.

5. Continued studies to develop sensitive and specific diagnostic tests for antibodies to detect early infection.

6. Initiated or expanded studies of dual infections with HIV-1 and HIV-2 through Projet Retro-C.I. in Abidjan, Cote D'Ivoire, West Africa.

7. Continued studies to better understand animal models of HIV and Simian Immunodeficiency Viruses (SIV) to define the pathogenicity and significance of immune responses to these viruses.

8. Provided ongoing consultation and laboratory support to assist producers of HIV antibody tests, manufacturers of prophylactic and therapeutic agents, and other organizations in their continuing development of new diagnostics, treatments, and potential vaccines.

9. Continued to provide extensive support to AIDS epidemiology, surveillance, and research projects.

10. Enrolled over 1400 laboratories in the CDC voluntary AIDS Performance Evaluation Program.

IMPLEMENTATION OF PREVENTION STRATEGIES

C. Implementation of Prevention Strategies

1. Developed a cooperative agreement to support 64 minority and other community-based organizations (CBOs) in 27 metropolitan

statistical areas (such as New York City, Los Angeles, Chicago, Boston, etc.) with the highest number of reported AIDS cases. More than half of the $9.9 million was awarded to CBOs which represent and serve racial and ethic minority populations.

2. Implemented a program to support initiatives in 53 State and local health agencies to prevent HIV in racial and ethnic minority populations. More than 281 organizations received support through this funding mechanism.

3. Co-sponsored the third National AIDS Conference on the Prevention of HIV Infection and AIDS in Racial and Ethnic Minorities in August 1989.

4. Implemented a National and Regional Grant Program for Minority Organizations and awarded 32 grants for a total of $6.2 million.

5. Provided support and technical assistance to the United States Conference of Mayors for seed funding and technical assistance to 23 minority community-based organizations in fiscal year 1989.

6. Provided support to fund health education/risk reduction, counseling and testing, partner notification, public information activities and racial and ethnic minority initiatives in 63 States, cities, and territories and consolidated their funding into one cooperative agreement with the previously separate Surveillance Cooperative Agreements. Provided support to extend counseling and testing activities to STD, TB, drug abuse and women's and children's clinics. In fiscal year 1990, 65 States, cities and territories will be funded.

7. Monitored and provided technical assistance to eight cooperative agreements with States, localities and another non-profit entities to implement and evaluate approaches to preventing perinatal transmission of HIV infection.

8. Provided continuation support to seven community-based demonstration projects to allow the assessment and validation of intervention strategies for use in ongoing programs.

9. Provided continued technical support, in collaboration with HRSA and the National Hemophilia Foundation, for targeted health education and risk reduction efforts directed to persons with hemophilia and their sex partners.

10. Developed, in concert with HRSA, professional training programs for health care professionals to permit health care delivery systems to respond to the needs for information as well as technical services.

11. Established an interagency agreement with HRSA to support pilot programs for HIV prevention and treatment in community health centers.

12. Developed protocols for studies to evaluate the impact of HIV counseling and testing in drug treatment centers and to evaluate the effectiveness of partner notification in a variety of settings.

13. Integrated specialized counseling information and skills into ongoing public health training programs associated with the HIV epidemic, and developed and delivered specific educational and training seminars to respond to scientific breakthroughs.

14. Provided support to 20 national education and health organizations that work to increase the number of schools and youth serving agencies providing HIV education for youth. In 1989, many national organizations developed and disseminated materials to inform the Nation's educators about the need for HIV school health education and the role that educators, school superintendents, school boards, and others can play to support schools in their HIV education efforts.

    For example, the National Association of State Boards of Education (NASBE) published Someone at School Has AIDS: A Guide to Developing Policies for Students and School Staff who are Infected with HIV. To develop the guide, NASBE convened experts in medicine, public health, education, and law. The guide recommends scientifically and legally based policy statements that State and local departments of education can use in developing policies for HIV-infected students and staff.

15. Provided support to State and local departments of education to help schools implement HIV education programs. In 1989, virtually every State department of education in the country provided teacher training programs to enable them to teach students about HIV. For example, over 12,200 teachers, school administrators, school board members, and parents were trained through 6 AIDS regional training centers established by the New York State department of education.

16. Expanded a materials development and dissemination system to identify, develop, and provide information about interventions that can be used to help school and college-aged populations avoid risks for HIV infection and other important health problems. These materials include curricula, films, videotapes, audio tapes, policies on health education, policies on disease and injury control, books, teacher training programs, materials for parents, brochures, etc. Over 400 abstracts describing these materials have been entered into a database for easy access by educators.

17. Provided support for training and demonstration centers to train school and community personnel to implement state-of-the-art interventions that can help young people avoid risks for HIV infection and other important health problems. Two centers provide training for State-based teams from across the Nation, while one center emphasizes training of city-based teams. Twelve smaller regional training centers train school and community personnel in their regions to implement comprehensive school health education curricula.

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18. Expanded the surveillance system for assessing school-based HIV education programs so that funded State and local departments of education will be able to determine the number and percentage of: 1) schools that provide HIV education at each grade level; 2) students that receive HIV education at each grade level; and 3) schools that provide HIV education within comprehensive school health education programs. In addition, 42 State and 15 local departments of education conducted surveys to assess HIV-related knowledge and beliefs among samples of high school students in their jurisdictions. Finally, a similar survey was conducted of a national sample of high school students in the United States to assess on a national level HIV-related knowledge and beliefs.

19. Continued development of an evaluation research system by offering two training conferences to help State and local Departments of Education evaluate and consequently improve their efforts to reduce risks for HIV infection and other health problems, to conduct research about the effectiveness of specific disease interventions, and to identify principal determinants of HIV-related and other health risk behaviors.

20. Established a survey research system to: (1) monitor State policies to protect and improve the health of students; (2) to help State and local departments of education monitor the percentage of students who receive HIV education and comprehensive school health education; (3) to help State and local departments of education monitor the prevalence of HIV-related and other health knowledge and health risk behaviors among high school students over time; and (4) to monitor the prevalence of HIV-related and other health knowledge and health risk behaviors among national probability samples of high school students over time.

21. Established an evaluation research system to help State Departments of Education evaluate and consequently improve their efforts to reduce risks for HIV infection and other health problems, to conduct research about the effectiveness of specific disease interventions, and to identify principal determinants of HIV-related and other health risk behaviors.

22. Developed and disseminated "Guidelines For The Prevention Of Transmission Of Human Immunodeficiency Virus and Hepatitis B Virus to Health-Care and Public-Safety Workers" and "A Curriculum Guide For Public-Safety and Emergency-Response Workers" within 90 days as required by "The Health Omnibus Programs Extension Act".

23. Utilized the National AIDS Hotline System including its Hispanic service and a TDD service for the hearing impaired to answer approximately 2 million calls.

24. Established, in collaboration with other Public Health Service agencies, the clinical trial and drug protocol toll free telephone information service for public access.

25. Developed and implemented a parents and youth focused public information program.

26. Awarded grants to 10 national organizations to expand prevention efforts to selected populations.

27. Provided funds to non-Federal, private sector organizations to facilitate conferences and workshops on HIV prevention and to provide scholarships for increasing attendance of racial and ethnic populations minority and people with AIDS. Organizations funded included National Aids Network, National Association of People with AIDS, Americans for a Sound AIDS Policy, and Eagles Foundation (minority ministers).

28. Received, since October 1987, over 36.8 million dollars in free public service television airtime for the National Public Information Campaign. Numerous prestigious awards were received in fiscal year 1989 by the Campaign including: (1) a Silver Anvil Award from the Public Relations Society of America, for the second consecutive year, (2) two CEBA awards -- (Communications Excellence to Black Audiences), and (3) a CLIO award for Hispanic messages.

29. Supported the Public Health Service's AIDS Awareness Month -- October 1989--and the World Health Organization's World AIDS Day on December 1.

30. Distributed technical information products, including over 190,00 slides, to the scientific and educational communities.

31. Published and disseminated 13 MMWR articles (in final and camera-ready form) containing guidelines and recommendations concerning the prevention and control of HIV infection.

32. Provided speakers for educational institutions and numerous National, State, and local professional and lay audiences.

33. Responded to approximately 13,000 telephone calls to CDC directly from the public and health professional communities with questions or comments on AIDS (by recording and by individual response).

34. Granted numerous interviews with representatives of the print and electronic media.

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CENTERS FOR DISEASE CONTROL

National Center for Health Statistics

HIV RELATED ACTIVITIES

National Health Interview Survey

A special 15-minute questionnaire on AIDS and HIV is administered to one adult respondent in each household as a component of the National Health Interview Survey (NHIS). The NHIS collects health data in about 50,000 households each year, with a response rate of over 95 percent. About 800 HIV questionnaires are completed each week, and results are published in the Advance Data series, currently on a quarterly basis. This study was added to the NHIS in August 1987 and will continue with periodic modifications to the content. Information is obtained on knowledge about HIV transmission, HIV testing, assessment of risk and prevention of HIV.

National Mortality Data

Mortality data for HIV infection from the national vital statistics system (NVSS) are based on a new coding and classification system developed by the National Center for Health Statistics and the Center for Infectious Diseases -- both of the Centers for Disease Control. Beginning with deaths occurring in 1987, final mortality data for HIV infection are published annually in summary in the Monthly Vital Statistics Reports (MVSR) and subsequently in the Vital Statistics of the United States. More current provisional estimates of HIV-related and other cause-specific mortality are published monthly in the MVSR three to four months after the date of occurrence.

According to final mortality data from the NVSS, there were 13,468 deaths due to HIV infection in 1987. The age-adjusted death rates and almost all age-specific death rates were highest for black males, followed by white males, black females, and white females. For the total population, HIV infection ranked as the 15th leading cause of death in 1987; it was the 10th leading cause for the black population and did not rank among the 15 leading causes of death for the white population.

National Hospital Discharge Survey

The National Hospital Discharge Survey adopted the new International Classification of Diseases codes for HIV in October 1987. This continuous survey makes estimates of the number of hospital discharges, and related characteristics such as length of stay, from information abstracted from records in a sample of short-stay hospitals. Data on "AIDS-related" discharges are published in the Advance Data series.

National Mortality Followback Survey - 1986

THe National Mortality Followback Survey is based on a one-percent sample (about 20,000 deaths) of 1986 death certificates with information about the decedent collected in a mail questionnaire. Information is obtained about socio-demographic characteristics, utilization of services during the last year of life and health behaviors. An Advance Data report entitled "Characteristics of Persons Dying from AIDS" was published in August 1989.

National Survey of Family Growth - 1988

The National Survey of Family Growth is a periodic household interview survey of women of childbearing age designed to monitor changes in childbearing practices and to measure reproductive health. The 1988 survey of 8,450 women included questions on awareness of sexually transmitted diseases (including HIV), and changes in sexual behavior to avoid such diseases, as well as questions assessing the likelihood of getting HIV. This survey routinely collects data on sexual partner history. HIV-related data will be published in 1990. In early 1990 women interviewed in 1988 will be reinterviewed by telephone to monitor changes in fertility, contraceptive practices, and knowledge and attitudes about sexually transmitted diseases, including HIV infection.

National Maternal and Infant Health Survey - 1988

The periodic National Maternal and Infant Health Survey (NMIHS) is based on a sample of about 20,000 birth certificates and fetal and infant death records. Questionnaires are administered to the mothers and health care providers associated with the births and deaths. Physicians are asked if the mother was tested for HIV (and the results) and the hospital is asked what tests were performed on the infant. A provisional data tape was released to NMIHS cosponsors in December 1989, and data will be published from the survey in 1990.

National Health and Nutrition Examination Survey III - 1988-1994

The National Health and Nutrition Examination Survey III is collecting data through direct physical examinations of 30,000 persons during the period 1988 - 1994 in mobile examination centers. A sample of the blood drawn from adults will be blinded and anonymously tested for HIV status. Results from the first half of the sample will be available in 1992.

National Ambulatory Medical Care Survey - 1988

The National Ambulatory Medical Care Survey collects data about physician visits from a sample of physicians. The 1989 survey will include on the data collection form questions about whether the patient was counseled about HIV and if an HIV test was performed.

National Household Seroprevalence Survey

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In mid-1988 a study was begun to determine the feasibility of a national household survey to measure HIV infection in the U.S. population. A pilot study of 300 households, conducted in Allegheny County, Pennsylvania, was completed in February of 1989 with a participation rate of approximately 80%. Based on the procedures developed during the pilot, a second larger test was conducted in Dallas County, Texas. The field work began in late September and ended in late December 1989. This study will produce an HIV seroprevalence estimate for Dallas County. Data from a quality assessment study conducted as part of the Dallas survey will help in assessing the validity of the estimate. A final report will describe the study and assess the technical feasibility of the national survey. The report will be available by mid-1990.

Methodological Research on Improving Survey Response to Sensitive HIV-related Topics

NCHS is expanding its cognitive research in questionnaire development in the area of HIV-related surveys to improve the reporting of sensitive, high risk behaviors in surveys. This effort is critical to measuring the patterns and distributions of high risk behaviors and in evaluating the impact of HIV education programs. Plans include developing an inventory of HIV-related questionnaires to increase the collaboration of HIV researchers and further enhance the comparability of surveys.

ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION

National Institute on Drug Abuse

DRUG ABUSE AND AIDS

In the United States, drug abuse is the second leading risk factor for acquiring HIV in adults, the primary risk factor for HIV seropositivity in infants; and, through pre- and perinatal effects including AIDS, the ninth-ranked killer of children under the age of five. In response to these critical and deadly links between drug abuse and AIDS--links which have been recognized by the National Academy of Sciences, the President's Commission on AIDS, and the Surgeon General--the National Institute on Drug Abuse supports a broad spectrum of AIDS-related research. Areas of emphasis include natural history and epidemiology of drug abuse and AIDS, treatment improvement, clinical research, and diverse educational and behavioral prevention/intervention efforts. One measure of the productivity of NIDA's effort is seen in the presentation of more than 100 NIDA-funded research reports at the 1989 Montreal International AIDS conference.

Epidemiology of AIDS:

Concomitant with the initial case reports of AIDS among homosexual men were reports of Pneumocystis carinii pneumonia among men who denied homosexuality but admitted to intravenous drug abuse. Initially, skeptics assumed that these cases involved male prostitution in order to procure drugs. Only as case reports among male intravenous drug abusers continued, and as female cases were reported, did it become clear that intravenous drug abusers were also at risk for AIDS. Intravenous drug abusers now account for about 30 percent of all AIDS cases in the U.S.

As of September 30, 1989, 109,167 AIDS cases in the United States have been reported to the Centers for Disease Control (CDC). Each day, about 100 new AIDS cases are reported to CDC. AIDS cases may be categorized, or described, by combinations of (1) history of intravenous drug (IV) abuse, (2) sexual orientation, (3) sex, (4) race, (5) geography or location, (6) history of sexual contact with members of other risk groups, and (7) history of other routes of exposure to blood or blood products, e.g., transfusion. Information is not available concerning risk for AIDS associated with all combinations of these factors. However, the over-representation of AIDS cases among demographically defined subgroups reveals much about the interrelationships among drug abuse, sexual transmission, and AIDS. The following section summarizes epidemiologic findings particularly pertinent to the interaction of intravenous drug abuse with the seven factors.

Drug Use: Of AIDS cases involving IV drug use (i.e., 30 percent of all cases reported to CDC) heterosexual intravenous drug abusers account for approximately 75 percent, and homosexual and bisexual IV drug users account for the remainder. Among male

AIDS cases, 17 percent were heterosexuals who reported that at least once prior to developing AIDS, they had used needles for self-injection of drugs not prescribed by a physician. Fifty-two percent of all female AIDS cases reported such a drug abuse history.

Race: According to the 1980 U.S. Census, whites account for approximately 80 percent of the U.S. population, blacks 12 percent, and Hispanics 6-percent. Whites account for 72 percent of AIDS cases among homosexual/bisexual men; 76 percent of cases among hemophiliacs and blood transfusion recipients; and 20 percent of cases among heterosexual intravenous drug abusers with AIDS.

The distribution of AIDS among blacks and Hispanics differs considerably. Blacks account for 50 percent of AIDS cases among heterosexual intravenous drug abusers; for 63 percent of cases attributed to heterosexual transmission; and for 60 percent of cases attributed to perinatal transmission. Within the Hispanic population, the percentage of heterosexual intravenous drug abusers and children with perinatally-acquired AIDS (29- and 26 percent, respectively, of total reported cases) exceeds rates among whites (20- and 14 percent, respectively).

Geography: While All 50 states, Puerto Rico, and the District of Columbia have reported at least one AIDS case among heterosexual intravenous drug abusers, heterosexual IV drug abuse-related AIDS cases predominate on the East Coast. New York and New Jersey account for over 60 percent of all cases among heterosexual intravenous drug abusers. These same two States account for only 22 percent of homosexual IV drug abusers with AIDS and 25 percent of all AIDS cases not reporting intravenous drug abuse. On the West Coast, the situation is entirely different. In California, for example, heterosexual IV drug abusers with AIDS account for only 3 percent of all cases.

Sexual contact across risk groups: Although only 5 percent of AIDS cases can be attributed solely to heterosexual contact, many of these can be directly linked to intravenous drug abusers. Likewise, 81 percent of pediatric AIDS cases can be attributed to a mother who is an IV drug user or the sexual partner of an IV drug user. Fifty percent of the mothers of children with perinatally acquired AIDS were IV drug abusers; an additional 20 percent of these mothers were heterosexual contacts of IV drug abusers. Forty-nine percent of AIDS patients whose cases were attributed solely to heterosexual transmission reported sexual contact with an IV drug abuser. Among the heterosexual partners and children of IV drug abusers, AIDS is occurring in epidemic fashion. While AIDS has been reported among intravenous drug abusers in Africa, Asia, Europe, Oceania, and South America, the proportion of total cases attributed to IV drug use varies regionally.

In order to reasonably estimate the number of drug abusers who are at risk for AIDS by needle sharing, it is important to define the population being counted. Unfortunately, definitions used to make these estimates are not always consistent, and conflicting numbers sometimes appear. The original (1986) Public Health Service estimate of IV drug abusers cited 750,000 regular users and 750,000 occasional IV drug abusers.

In a 1987 estimate compiled by the National Association of State Alcohol and Drug Abuse Directors, Inc. (NASADAD), the total number of IV drug users in 35 States, the District of Columbia, and Guam was judged to be 1.4 million; it is noteworthy that fewer than half of the responding State agencies based their estimates on data; the remainder were "guess-timates."

Given these deficiencies in data needed by researchers as well as planners and policy makers seeking to understand the human and societal costs of the rapid spread of HIV infection and AIDS, NIDA's AIDS computer modeling programs are exploring extant data sets to determine their strengths and weaknesses in answering basic questions about the spread of AIDS. Where gaps are seen in these data sets, recommendations will be made for upgrading them.

Clearly, communication and sharing of data is a major challenge in AIDS research. Recently, a NIDA-supported international modeling program has established a cooperative system of mathematical and software development involving three sites--two in the U.S. and one in Canada, with a fourth site from the United Kingdom planned. The economies of scale and efficient and timely sharing of data through computer links in this project serve as a model for timely communication and data storage.

Prevalence:
Simply counting the number of AIDS cases does not adequately describe the extent of the problem. AIDS is caused by HIV, a virus that is transmitted from person to person through sexual contact, exposure to infected blood and blood products, and from mother to child during pregnancy. Because of the long latency period from infection to diagnosis of AIDS, and the persistence of infectivity of HIV-antibody positive individuals, the number of infected individuals is considered to be a better measure of the extent of the epidemic among intravenous drug abusers. Unfortunately, current information about HIV seroprevalence among IV drug abusers is limited.

Investigators from CDC and NIDA have collaborated to review 92 published and unpublished studies of the prevalence of HIV infection among IV drug abusers in the U.S. HIV seroprevalence among IV drug abusers in drug treatment programs ranged from zero to 65 percent. Seropositive rates were highest in New York, New Jersey, and Puerto Rico, and lowest in smaller cities in the West, the Midwest, and the South. Heightened risk of infection was associated with black and Hispanic ethnicity.

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That HIV seropositivity in a population of IV drug abusers tends to increase over time has been demonstrated in a study of heterosexual men and women in New York City who were current or former intravenous heroin abusers, were on methadone maintenance, and were enrolled in a study of chronic liver disease. Stored sera from participants were tested for HIV antibody. In 1978, none of the sample were HIV positive; for 1979, 29 percent were HIV positive; for 1980, 44 percent; for 1981-83, 52 percent; and by 1984, 56 percent.

Within a given city, moreover, HIV seroprevalence among IV drug abusers may vary by drug-using behavior, race, sexual orientation, and treatment facility. In a San Francisco study in which 281 heterosexual intravenous drug abusers recruited from five major opiate addiction treatment programs were tested, 10 percent were seropositive for HIV antibody. Addicts who reported sharing needles with two or more persons were more likely to be positive than those who did not report sharing needles; and blacks and Latino participants were more likely to be positive than whites.

Treatment for drug abuse also affects seropositivity. In another study conducted in San Francisco, 401 intravenous drug abusers were screened for HIV antibodies and interviewed concerning their medical, sexual and drug use histories. Subjects included 300 participants in a 21-day detoxification program and 101 IV users who were not in treatment. Seven percent of the detoxification patients and 16 percent of the not-in-treatment participants were HIV seropositive.

Natural History: Natural history studies are longitudinal, prospective, epidemiological studies designed to identify the time course and prognostic factors associated with progression of HIV disease from HIV infection, measured by seroconversion, through acute retroviral syndrome, asymptomatic periods, non-AIDS defining illnesses, AIDS, and death.

One purpose of natural history AIDS studies is to identify "cofactors." A cofactor in AIDS is a non-HIV-related influence that "operates" in conjunction with HIV to affect the progression of AIDS and diseases associated with it. Identifying cofactors in AIDS could prove invaluable in developing strategies to prevent or slow disease progression.

Illicit drugs may act as a cofactor in the development of AIDS. Because of the high frequency of AIDS among intravenous drug abusers and homosexual men who reported use of large amounts of drugs before developing AIDS, some investigators have speculated that drugs of abuse may expedite the disease process or lead to specific outcomes, such as Kaposi's sarcoma (KS) or non-Hodgkin's lymphoma, both of which are regarded as AIDS-defining illnesses. It has been hypothesized that certain drugs of abuse act as immunosuppressants, compounding the effects of HIV-induced immunosuppression. It also has been suggested that alcohol and

other drugs of abuse decrease one's ability to resist risky sexual or needle-sharing behavior that could result in HIV infection.

In 1986, NIDA developed an investigator-initiated grant program to evaluate these and other hypotheses related to the natural history of HIV infection among drug abusers and to compare the observed progression of disease with that observed in other populations. The Institute currently is supporting 20 longitudinal studies of cohorts of IV drug abusers, involving over 20,000 subjects recruited from drug treatment, the criminal justice system, sexually transmitted disease clinics and hospitals, and/or "the street." Principal investigators consist of epidemiologists, infectious diseases physicians, psychiatrists with drug abuse treatment backgrounds, psychopharmacologists, and social scientists with prior experience conducting drug abuse research. Psychosocial characteristics, risk behaviors, medical history, neuropsychological and neurophysiological measures, physical examination, and clinical status will be evaluated. Study results will suggest various intervention foci and future research initiatives.

Increasing evidence points to presence of a cofactor in the development of Kaposi's sarcoma in AIDS. The cofactor appears to be highly associated with the homosexual male lifestyle, to be on the decrease among gay men with AIDS, and to occur more commonly among white homosexual men on the East and West coasts than among black and Hispanic homosexual men. The cofactor does not appear to be blood-borne or sexually transmitted. The abuse of nitrite inhalants have been proposed as a possible cofactor in AIDS-related Kaposi's sarcoma and as an explanation for the unique epidemiology of this cancer in HIV disease.

Prevention Strategies: In the absence of a vaccine to prevent the spread of HIV infection, behavior change is the primary means of prevention available. Accordingly, research that contributes to the identification of effective behavior change strategies is a NIDA priority. One aspect of AIDS prevention research focuses on understanding the determinants of the initiation and maintenance of risk-taking behaviors. Determinants of behavioral choice, response effort and complexity, the effects of drugs on control of behavior by non-drug environmental stimuli, procedures to increase the salience of the negative consequences of risky behavior, and the positive consequences of safer practices are among numerous variables that require further investigation.

Intervention strategies must address needle use and sexual behavior to reduce the risks of contracting or transmitting HIV. Most needed are interventions that will achieve multiple behavior changes, maintain them over time, and, through replication studies, be shown applicable to diverse populations. Community-based interventions must incorporate outreach strategies. NIDA also emphasizes interventions designed to prevent the progression from initial drug use to intravenous drug use, particularly among

high risk youth, and strategies designed to research "elusive" populations. This latter need poses tremendous challenges to the field. AIDS prevention requires consistent changes in what are often deeply rooted, culturally supported, private behaviors. In the case of intravenous drug abusers and their partners, these may include unsafe sexual practices as well as drug and needle using behaviors. Also, for many hard-to-reach individuals, risk-taking is part of their daily lives. AIDS is an additional threat to life, but may not be viewed as the most immediate or serious problem they face.

Social and physical environments must be considered in developing prevention strategies. In some New York City neighborhoods where abandoned buildings are readily available to serve as "shooting galleries," rented needles or "works" may be shared by more than 100 individuals on a given day. In other communities, IV drug users may share needles only among friends. Also, access to sterile injection equipment, as well as the criminal penalties for possessing or using such equipment, vary from place to place, as does knowledge about risk for HIV infection among intravenous drug abusers. Such variations point to the need for prevention strategies tailored to different social contexts and groups. To this point, since rates of AIDS associated with IV drug use is far higher among blacks and Hispanics than among whites, it is crucial that prevention programs be sensitive to ethnic, cultural, and linguistic contexts.

Intravenous drug abusers are engaged in a behavior that is not only stigmatized, but also illegal. Often, sexual partners of IV drug abusers are also stigmatized and isolated. Thus, it is extremely difficult for these individuals to organize themselves to support and direct behavior change within their communities. As a group, IV drug abusers and their families, as compared to homosexuals, lack political and voluntary organizations, a community press, or an established system of support and resource programs. These realities require that behavior change programs be brought to the IV drug abuser and to the community he or she places at risk.

Intravenous drug abusers who enter drug abuse treatment programs take a major step toward limiting their own, and their community's risk for AIDS. Treatment programs routinely provide information about AIDS and its threat, and offer the path to a drug-free lifestyle. Much of the educational programming for treatment staff is grounded in training programs developed by NIDA. There is need, however, to look beyond the present drug abuse treatment system. For instance: 1) an estimated six out of every seven drug abusers are not in treatment; 2) there are not enough treatment slots to accommodate all those seeking treatment--in fact, there are waiting lists in many urban areas of the United States -- particularly in cities in the Northeast; and 3) even if enough treatment slots were immediately available, many IV drug abusers will fail in treatment and relapse.

Adolescents require special prevention efforts. At least half of all high school seniors have tried an illegal drug, and an even higher proportion of adolescents who are school drop-outs or who are involved in other deviant behaviors are believed to have tried illegal drugs. Longitudinal studies show that use of drugs during adolescence predicts continued use adult use, and suggests transition from non-intravenous to intravenous methods of use. Sexual intercourse and continued high-risk sexual behaviors (number of sexual partners, number of anonymous sexual partners, failure to use birth control or prophylaxis) are common among large numbers of adolescents.

Further compounding prevention efforts are research findings which demonstrate that drug abusers are not "single drug" users or even "single route" users. While information regarding HIV seroprevalence among non-IV drug users is sparse, HIV is likely to spread rapidly among sexually promiscuous drug abusers, ever those who do not inject drugs. Research must examine how the "real life" patterns of drug abuse and its associated sexual behavior affect HIV transmission.

Studies to Improve Treatment Effectiveness: HIV infection can be prevented now. It requires practicing "safe" sex and either the non-use of needles, or at a minimum, the use of new or sanitized needles. While drug abuse treatment offers effective means of educating addicts, effecting behavior change, and reducing or eliminating drug use, a number of problems exist with current treatment approaches. These problems include unacceptably high client dropout rates, continued drug use during treatment, and high relapse rates following treatment. Overcoming these problems is expected to make drug abuse treatment an even more effective AIDS prevention strategy.

NIDA supports a number of research efforts to improve treatment effectiveness. These include: 1) an initiative to demonstrate that improved treatment significantly reduces the spread of AIDS, 2) a longitudinal study of treatment outcomes, 3) development of pharmacotherapies, and 4) development of psychosocial approaches.

Reducing Risk of AIDS Through Treatment: Research is underway to demonstrate that improved drug abuse treatments result in greater decreases in AIDS-risk behaviors than pre-improvement treatments. All forms of drug abuse are targeted, including IV use of opiates and/or other drugs, as well as types of drug abuse that frequently involve unprotected sex in exchange for drugs or money to purchase drugs.

Diseases other than AIDS are also closely associated with IV drug abuse, including hepatitis, endocarditis, and tuberculosis. Recent outbreaks of syphilis and gonorrhea have been associated with cocaine (particularly "crack") abuse. Adverse fetal and child developmental effects may result from maternal drug abuse during pregnancy. By focusing more attention on these diseases, drug abuse treatment programs may become more sensitive to the

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medical needs of clients, thus making drug abuse treatment more attractive to drug abusers and, hopefully, enhancing treatment retention.

Treatment Outcomes: In order to follow persons in treatment over time, NIDA recently implemented the Drug Abuse Treatment Outcome Study (DATOS), which will collect and analyze treatment admission and outcome data over a 5-year period. The study will follow 20,000 individuals coming into five treatment modalities in 50 treatment programs offering short- and long-term methadone maintenance, short- and long-term residential treatment, and outpatient drug-free treatment. Of these 20,000 individuals 4500 will be selected for a follow-up interview and study. DATOS--the first large-scale study of treatment outcomes since the implementation of block-grant funding will yield valuable information about the characteristics of individuals in treatment and the effectiveness of current treatment programs.

Psychosocial Approaches: NIDA's drug abuse treatment research portfolio includes efforts to develop innovative, effective and cost-efficient psychological/psychosocial therapeutic approaches. Areas of emphasis in treatment research program have included:

- interrelations between drug abuse and other biobehavioral disorders (e.g. eating disorders and stimulant abuse);
- problems of specific populations;
- special problems related to particular agents (e.g. cocaine) or forms of drug abuse; and,
- interactions among behavioral, pharmacological and treatment variables.

Overall, there have been direct efforts to better understand antecedents to treatment, treatment processes (i.e. what goes on in treatment) and the outcome of treatment.

In all areas of treatment research, there is a continuing need to bolster programs and opportunities for training of scientists and clinicians.

With the exception of heroin addiction, most abused drugs have no well-accepted pharmacological treatment; even when one is available, it is limited in its applicability and its effectiveness. Persons typically come to drug abuse treatment with significant medical, psychological, and psychosocial problems in addition to use of illicit drugs. Whether drug abuse is a cause, an effect, or unrelated to such problems, studies have shown that these problems must be treated in conjunction with the drug abuse to reduce the likelihood of relapse. Psychosocial intervention often is the primary, if not the only, treatment for the drug abuse as well as concomitant disorders.

Biomedical Research: A major concern in treating AIDS is the effect of abused drugs and agents used therapeutically in drug abuse treatment on immune function. It is hypothesized that drug

abuse may affect immune function, thus contributing to HIV infection and disease progression. Immunological research is underway to study the effects of drugs of abuse on the immune system and the interaction of these effects with HIV. The determination of vulnerability to initial infection and to the disease manifestations of HIV will be assessed subsequently. Immunological factors influencing the vulnerability of drug-abusing minority populations are particularly important. Studies will attempt to separate other manifestations of the drug-abusing life style (e.g., malnutrition and other infections) from the primary effects of drugs and HIV.

Clinical studies examining the immunologic effects of opiates, marijuana, and other abused drugs on immune functioning are being expanded. Research, to be conducted predominately in humans, will examine effects on the immune system of: 1) specific drugs and patterns of drug abuse; 2) medical conditions and illnesses associated with drug abuse; 3) pharmacotherapeutic agents used for HIV and drug abuse treatment (e.g., AZT, methadone, naltrexone, LAAM, buprenorphine, clonidine, antidepressants); 5) biological and/or genetic factors known to be involved in drug abuse (e.g., age, sex, race/ethnicity); and 6) environmental factors such as nutrition and exposure to toxic agents. Research on the effects of psychosocial stressors and HIV-induced organic stress on immune functioning is also important.

Preclinical research supports and complements clinical studies. Research emphases include:

1) the identification and study of physiological, biochemical and immunological mechanisms in the pathogenesis of drug-modulated HIV encephalopathy;
2) the effects of stress on the immune system and endocrine function, and the effects of abused drugs on stress factors;
3) definition, characterization and approaches to evaluating effects of abused drugs on cellular toxins, lymphokines, receptors and other cellular functions affected by HIV infection; and,
4) elucidation of the hypothalamic and immunologic control of drug-modified HIV neurologic changes as reflected by physiologic, behavioral, genetic, and biochemical measures.

These studies will be predominantly conducted in animal models and/or with the use of isolated tissues.

Community-Based AIDS Prevention Research: The spread of HIV has slowed among homosexual and bisexual males, but is increasing rapidly among IV drug abusers and their contacts. In 1987, less than one-quarter of AIDS cases reported to CDC were individuals who had used drugs intravenously; in 1989, that figure rose to 30 percent. The vast majority of AIDS cases among both women and children are linked, either directly or indirectly, to intravenous drug use.

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In 1986 and 1987, NIDA sponsored a national demonstration research effort to implement and evaluate different outreach, AIDS education, and behavioral change intervention methods targeted to intravenous drug abusers and their sexual partners in the community setting. This program funded additional projects in September 1988, with greater emphasis on reaching pregnant women and their partners, prostitutes, and runaway or homeless youth who are intravenous drug abusers or sexual partners of intravenous drug abusers. NIDA's AIDS demonstration research programs--funded through 29 grants and 12 contracts--currently are operating in 63 sites throughout the mainland United States, Hawaii, Puerto Rico, and along the U.S.-Mexico border.

Typically, these initiatives rely on outreach staff who know, and are known within, their communities. When initiating community-based projects, sensitivity to ethnic, cultural, and social stresses is crucial if trust is to be built between the treatment community and the clients its serves. It is the task of outreach staff to locate individuals at high risk who might otherwise be overlooked in prevention efforts, especially IV drug abusers who are not in contact with the drug abuse treatment system or other traditional service delivery systems, along with their sexual partners and children who are at high risk for AIDS.

Research demonstration participants receive a standardized structured interview at intake. This interview collects information about behaviors related to drug and needle use, sexual practices, use of community health and service agencies, mobility, HIV testing, health status, knowledge regarding AIDS and means of infection, and demographic characteristics. After collecting baseline data and making HIV testing available, participants are randomly assigned to either a "standard" or an "enhanced" intervention, and re-interviewed at six-month follow-up to assess changes in behaviors and knowledge.

The standard intervention is typically comprised of an AIDS educational session with referral for needed community services. The enhanced interventions may include, in addition, any of the following interventions:

- Individual and group counseling designed to encourage behavioral change;
- Couples counseling, in which intravenous drug users and their sexual partners are helped to understand the risks and explore alternative behaviors;
- Cognitive skills training, in which at-risk individuals are aided to explore means-ends relationships and consequences related to their own behaviors, and to develop and test out alternatives (Cognitive skills building often is conducted after efforts to induce participants' greater awareness and concern about their own vulnerability.);

- Peer networks, which are developed to support participants' efforts to reduce risk of HIV infection;

- Social skills training, in which sexual partners, in particular, are helped to explore and test strategies for asserting their own needs and for modifying the behaviors of others that place them at risk for HIV infection.

Baseline and follow-up instruments were developed collaboratively with project staff and experts in the field. The interview data are supplemented both by HIV test results and observational data recorded by program staff; these data will be linked to that provided by participants to provide a clear understanding of the target populations and their communities, the interventions, and program effectiveness.

To permit effective and efficient collection, monitoring, and analysis of field information, NIDA established a National Data Coordinating Center in September 1987 to synthesize and analyze data obtained through the research demonstrations. The Center also provides standardized interviewer training and coordinates field reliability and validity studies.

The demonstration research project has begun to yield important findings on intravenous drug abusers not in treatment and on the sexual partners of intravenous drug abusers. As of March 1989, responses of 4,824 intravenous drug abusers to the baseline interview schedule administered in 18 programs between mid-1988 and February 1989 had been analyzed.

Significantly, the reports from both intravenous drug abusers and their sexual partners indicate that these persons were knowledgeable about AIDS at the time of interview, but were continuing to engage in high-risk behaviors anyway. This finding is consistent with other findings from health education research. It is therefore apparent that knowledge alone is not sufficient to induce behavioral change.

Outreach research projects are now beginning to report early findings regarding the efficacy of their interventions. Programs in New York City, Chicago, San Francisco, San Diego, Laredo, and San Juan have identified impediments to effective outreach and ways for overcoming them. Programs in New York City, Chicago, Houston, Miami, and San Francisco report reductions in risk behaviors associated with needle use. From survey data collected during the past two years, San Francisco reported significant changes in risky behaviors related to HIV transmission. Safer needle hygiene practices increased from 39 percent to 70 percent, and condom use from 23 percent to 42 percent during the study period. New York reported that the mean monthly number of drug injections declined from 34 to 10 during a 140 day pre-post-survey period. Of those in the same survey who reported having had sex during the year before the first interview, 36 percent used a condom at least once. Of the same cohort

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interviewed 140 days later, 53 percent had used a condom at least once when having sexual activity during the intervening period.

Outreach intervention programs in Laredo, Texas; San Diego, California; and San Juan, Puerto Rico reported decreases in both unsafe needle use and unsafe sexual practices in all three cities between the six months before the first interview and the six months after the initial interview and program intervention. Over time, these and other ongoing NIDA programs will help to elucidate the needs and functioning of target populations, differences between subcultures that require special programmatic approaches, and strategies that work most successfully in locating different groups and in engaging them in behavioral change.

By bringing innovative and culturally-appropriate preventive interventions into the community, demonstration research programs have the potential for modifying unsafe drug use and/or sexual practices that place the individual and the community at risk. Through these projects, we are gaining a unique and unprecedented understanding of the characteristics and functioning of these populations outside of the treatment setting, the nature and extent of their risk-taking behaviors, and the prevention strategies that are and are not effective in reducing high-risk practices and promoting healthier lifestyles.

Refinement Of Evaluative Research Design: Since mid-1988, NIDA has refined research approaches to be used in assessing the efficacy of interventions, and has stimulated the development and documentation of promising intervention approaches. NIDA has worked collaboratively with existing programs to enhance the scientific rigor of their efforts and to chart future NIDA research. National and regional meetings have been convened to focus on specific tasks and develop recommendations regarding research in this area. Specific action has already been taken to:

- Develop and standardize an interview that is administered at fixed intervals pre- and post-intervention at all sites. Training and supervision are employed to ensure consistency among interviewers.

- Develop and implement quality control checks for interview data.

- Conduct reliability and validity tests of the instruments in use. Validity testing includes checking the consistency of responses to related items in the interview schedule and obtaining additional data on subjects' behaviors to relate to data obtained from interviews.

- Develop standard outcome measures for use across all projects and for all interventions. For example, standards are in place for reporting participants' HIV test results by

Western blot band (to allow for re-analysis, should new methodologies be developed for interpretation of band results).

- Develop a manual to assist programs in sampling and locating individuals for follow-up interviews.

Manuals and documentation are being prepared by projects to assure consistency in the administration of interventions and to permit the replication of interventions initially found to be effective. Findings will be communicated by NIDA to the drug abuse, public health research, and service communities, and will be used to update AIDS-related training programs.

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National Institute of Mental Health

ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

The Department of Health and Human Services has identified Acquired Immune Deficiency Syndrome (AIDS) as the foremost public health problem in the United States. The number of persons with AIDS continues to grow; as of November 1989, 115,158 cases of AIDS have been reported to the Centers for Disease Control (CDC). One new AIDS case is reported to CDC every eight minutes. At the same time, between one and 1.5 million Americans are estimated to be seropositive for human immunodeficiency virus (HIV); all these people, many of whom are unaware of their infected state, are potential transmitters of the disease.

The National Institute of Mental Health (NIMH) supports a broad, balanced program that addresses critical AIDS mental health research and training needs. The research program is responsive to the recommendations of the Public Health Service (PHS) and several major AIDS reports. The Charlottesville Report from the Second PHS AIDS Prevention and Control Meeting and the Presidential Commission on HIV Epidemic both highlight the need for research to fill gaps in knowledge in neurosciences, neurobiology, risk behaviors, and behavior change. The Institute of Medicine (IOM) report on Confronting AIDS: Update 1988 recommends long-term, comprehensive programs of research in the biomedical and social sciences intended to prevent HIV infection and to treat the diseases caused by it. In AIDS: Sexual Behavior and Intravenous Drug Use (1989), the National Research Council of the National Academy of Sciences recommended a series of activities to increase and improve programs of basic social and behavioral research related to HIV infection and AIDS.

The NIMH program involves research at the biological, psychological and behavioral levels, including basic research in neuroscience and behavior as well as clinical, services and prevention research. NIMH AIDS research focuses on: 1) CNS effects of HIV infection; 2) psycho-neuro-immunology; 3) clinical research on HIV-related mental disorders; 4) research on the structure, process and financing of mental health services for the mentally ill with HIV infection and those who develop mental health problems as a result of HIV infection; and 5) behavior change and prevention. NIMH supports grants for individual and institutional research training across all areas of NIMH AIDS research. The NIMH program also includes training of health and mental health care providers in the neuropsychiatric and psychosocial aspects of HIV infection. Recent training efforts focus on integrating AIDS mental health training into ongoing training of health care workers related to HIV.

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1989 Research Program

During FY 1989, NIMH expanded its support for intramural and extramural AIDS research, education, and training activities. In FY 1989, the NIMH AIDS program was approximately 72 percent investigator-initiated extramural research center grants and project grants, 11 percent intramural research, 13 percent program support contracts, 2 percent research training, and two percent research management and support. By program area, 43 percent of the FY 1989 AIDS expenditures focused on behavioral aspects of HIV infection, 32 percent on immunologic and neuroscience studies, 11 percent for the health care worker training program, 12 percent on natural history and co-factors, and two percent on mental health services research.

Extramural Research Program

An array of mechanisms has been used to provide support for extramural AIDS research. Currently, five multi- and interdisciplinary AIDS research centers are active. Seventy-two regular research projects, one program project, four scientist development awards, four small grants, and seven FIRST awards received support. NIMH also provides support for 17 institutional training grants and four fellowships to train investigators to conduct mental health AIDS research. The FY 1989 research budget totaled $41.3 million.

Support for four ongoing AIDS Research Centers continued in FY 1989. Centers were first established in cities with the highest AIDS prevalence rate; in FY 1986, centers were initiated at the University of Miami and at the University of California, San Francisco (UCSF). A third center was established at Columbia University in New York City in FY 1987. Support was provided for a fourth center at University of Michigan in FY 1988. The three initial Centers, New York, San Francisco, and Miami, are jointly sponsored by NIMH and NIDA. Funding was initiated in FY 1989 for a fifth research center at the University of California at San Diego.

Together the AIDS Research Centers are engaged in a broad range of research in the areas of CNS effects of HIV, neuropsychiatric aspects of HIV infection, psycho-neuro-immunology, and behavior change and prevention. Each center has a specific mental health theme and emphasis. In addition to conducting individual research projects, centers provide training to new scientists through a precepteeship program, a community core to work with relevant populations and community organizations, and information dissemination activities which promote rapid transfer of research findings to the local community and to practitioners.

The newly-funded HIV Neurobehavioral Research Center at the University of California at San Diego is examining the etiology, pathogenesis, and natural history of neurobehavioral disturbances associated with HIV infection. A unique contribution of this center will be research on military subjects for whom it is

possible to determine the exact time of seroconversion from seronegative to seropositive status. This will contribute to more accurately describing the effects of HIV seropositive status on cognitive functioning. Other projects will evaluate memory disorders in AIDS, explore the sensitivity of functional imaging methods as measures of HIV effects in the brain, and investigate interactions between depression and stress and the immune and nervous systems.

The Center for AIDS Prevention Studies (CAPS) in San Francisco is a confederation involving the University of California at San Francisco, the grantee, the University of California at Berkeley, the Bayview Hunters Point Foundation, a community based health and mental health setting with Black and Hispanic investigators, the San Francisco Department of Public Health, and San Francisco General Hospital. In addition to projects that address risk behaviors and prevention of HIV infection among Black, Hispanic, and White single men and women, the Center is supporting 25 innovative pilot studies to determine the most promising areas for future research.

The HIV Center for Clinical and Behavioral Studies in New York emphasizes prevention and clinical and behavioral studies of HIV infection and associated psychiatric disorders. The Center is located at the New York State Psychiatric Institute and collaborates with other departments, research centers, and hospitals affiliated with Columbia University, with the New York City Health Department, and with organizations that are concerned with HIV infection and AIDS in New York City. Research is targeted to school-based interventions, programs for high-risk adolescent street youth, and perinatal AIDS studies.

The Center for Biopsychosocial Study of AIDS located in Miami conducts coordinated multi-disciplinary research into the psychosocial, immunologic, neurophysiologic and neuropsychologic aspects of HIV infection in at-risk populations. For example, longitudinal studies are underway to assess the neurological and cognitive complications of pediatric HIV infection. Studies of intravenous drug abusers in the Black, White and Hispanic communities are also included in the center's activities.

The Midwest Biobehavioral Research Center (MABRC) at the University of Michigan, Ann Arbor, conducts research to assess the behavioral and psychosocial determinants and sequelae of HIV infection. MABRC is examining diverse outcomes of HIV infection (mental and physical health, AIDS-specific behaviors, psychoactive substance abuse, and immunological competency) as they may be determined by behavior and psychosocial factors.

Several collaborative efforts are underway to facilitate comparison of research results across centers and maximize findings. Workgroups with experts from each Center are assessing the state of knowledge and measurement issues in four areas: neuropsychologic/cognitive functioning, psychosocial aspects of

HIV infection, psychosexual behavior, and HIV infection in minority populations.

Extramural Research Findings - FY 1989

CNS Effects of HIV: Research evidence to date indicates that a large number of persons infected with HIV experience neurological, cognitive, and behavioral changes. Up to 60 percent of persons with AIDS may eventually develop AIDS Dementia Complex (ADC) and 10 percent of HIV-seropositive patients initially come to medical attention with neurological symptoms. HIV, the etiologic agent of AIDS, is neurotropic, entering CNS early in the course of infection. Clinical observations have demonstrated that CNS impairment is common by the time the HIV infection has advanced to AIDS. However, the precise cause of the neuropathology in HIV infection remains unknown.

- Studies from NIMH-supported AIDS Research Centers, as well as several individual research projects, suggest that HIV-infected individuals show deficits in cognitive and neuropsychological function. Preliminary research using an extensive cognitive battery with emphasis on verbal memory and processing speed has indicated that asymptomatic HIV-positive individuals show statistically significant memory deficits as well as a slowing in the processing of specific types of information compared with HIV-negative individuals. Intramural scientists are investigating possible mechanisms underlying the cognitive and other neuropsychiatric deficits seen in AIDS patients.

Behavioral Immunology/Psycho-neuro-immunology: Research has demonstrated that immune function can be influenced by neurological and psychological factors. Reciprocal relationships exist between the brain and immune systems, with the brain being the organ through which environmental and psychological factors influence the immune function. HIV affects both the nervous and the immune system, ultimately leading to progressive immune system failure and CNS degeneration, also known as AIDS Dementia Complex. Impairment of the regulatory feedback processes between the CNS and immune system could affect an individual's susceptibility to HIV infection, as well as the progression of the disease and development of neurological symptoms.

- Results from an ongoing study have shown that in mice, nerve cells of the autonomic nervous system directly innervate the spleen and lymph nodes. Using sophisticated immunocytochemical and neurochemical techniques, investigators are now examining how the release of the neurotransmitter norepinephrine from these cells regulates immune response through its influence on cell proliferation and distribution.

- Other factors which may alter immune responsiveness are being examined. Results show that Interleukin-1 (IL-1), a protein

that can function as mediator of immune suppression, is a potent stimulator of pituitary-adrenal activity. Additional research is investigating the specific area of the brain affected by IL-1 and whether this substance can activate autonomic pathways in peripheral immune organs.

Behavior Change/Prevention: Research on behavior change and prevention is a major focus of the NIMH AIDS Program. Since there is presently no vaccine for AIDS, NIMH AIDS prevention research has focused on behavior change and on developing methods to help people avoid specific sexual and drug-using behaviors that place them at risk for becoming infected. Data indicate that although some groups at high risk for HIV infection have changed behavior, a significant proportion have continued to engage in sexual and drug using behaviors that place them at high risk for AIDS. Interventions that appear promising in studies of gay men include cognitive behavior techniques, assertiveness training, skill training, and stress reduction.

- In a study of people presenting for HIV antibody testing, 88 percent of the non-monogamous sexually active participants reported that they intended to disclose a positive test result to a primary partner, and 74 percent intended to disclose to a non-primary partner. At the same time, people seeking antibody testing reported continuing to engage in activities that place themselves and others at risk for HIV infection. Of the sample, heterosexual men and women reported engaging in more high risk activities (i.e., intercourse without condoms) than did gay and bisexual men. People in this study generally understand the implications of a positive test result, and counseling does not increase knowledge concerning positive test results. However, people do not understand the implications of a negative test result (i.e., that one may not yet have seroconverted, that it could be a "false-negative" result) and counseling significantly affects this area of knowledge.

- Recent data from a study of a cohort of 700 gay men over the past five years indicates that high risk sexual behaviors have declined over time with the rate of such behaviors now appearing to level off. In the last year, 18 percent of the sample reported having engaged at least once in high-risk sexual behavior without a condom (compared to over 80 percent in 1981).

- Another study in three cities (Seattle, Tampa, and Mobile) focused on the differences between gay men who have reduced high risk behavior for HIV infection and gay men who are still practicing high risk sexual behaviors. Seventeen percent of the entire sample reported engaging in unsafe sexual practices in the preceding 3 months; 83 percent did not. Men who engaged in high risk sexual activities were more likely to attribute AIDS risk to chance/luck and "powerful other" external factors. They scored lower in AIDS risk knowledge,

were younger, and had less education than men who did not engage in this activity.

- A study of 453 gay and bisexual men followed from 1984 to 1987 found that 30 percent changed to and maintained low risk behaviors; however, 16 percent of the sample relapsed to high risk behaviors after initial behavior change, and another 4 percent maintained high risk behaviors throughout the study period. Approximately 50 percent of the sample maintained stable, low-risk behaviors throughout the study period.

- Preliminary findings from a research project evaluating a control group and a group of runaway and gay youths receiving an intervention at three community-based service agencies indicate: 1) sexual abstinence is higher for the first three months for the intervention group (19 percent% for control versus 54 percent for the intervention). This impact disappears at six months (36 percent of controls and 38 percent of the intervention); 2) the number of youths engaging in a "high risk pattern" is lower in the intervention group than in the control group.

Counseling/HIV Testing: From a primary disease prevention perspective, the behaviors that transmit HIV infection are modifiable. Counseling of HIV-positive individuals is one strategy to produce behavior change that will reduce the further spread of HIV. Effective prevention strategies require the cooperation and support of infected persons and their integration into adaptive social support networks, factors which are adversely affected by psychological distress and poor mental health functioning.

- The psychological effects of HIV testing in conjunction with individualized pre- and post-test counseling was assessed prospectively in a study in New York City. For HIV negative subjects, there was no difference in distress measures across three interventions: standard practice, interactive video, and a cognitive behavioral stress prevention program. Among HIV positive individuals, however, the cognitive behavioral program results in significant decreases in measures of depression and anxiety. This study suggests that HIV serological testing, when combined with individualized counseling, was emotionally helpful for both seronegative and seropositive research subjects at two months following notification.

Intramural Research Program (IRP)

The Division of Intramural Research conducts studies to understand the possible mechanisms underlying HIV-related behavioral and neuropsychiatric syndromes. The current research program of 24 AIDS-related investigations ranges from studying the basic mechanisms of HIV infection to the neuropsychological disturbances observed in many patients with AIDS. Projects include novel

attempts to inhibit HIV infection via receptor-based strategies, the elucidation of the possible neuropathological mechanisms of HIV infection, the neurochemical consequences of HIV infection that may contribute to neurotoxicity and neuropathology, and the development of suitable animal models of AIDS, as well as a series of carefully controlled studies of the impact of HIV infection on psychological and neurological function.

Intramural Research Findings FY 1989

- Quinolinic acid, which is normally present only in trace amounts in the brain, is a naturally occurring and potentially neurotoxic byproduct of the metabolic breakdown of tryptophan, an amino acid. Markedly increased levels of quinolinic acid have been found in the cerebrospinal fluid (CSF) of patients with AIDS dementia. CSF levels of this toxic metabolite correlate with dementia ratings of these patients, suggesting that quinolinic acid may play a role in the pathogenesis of AIDS dementia. Since quinolinic acid can be made by macrophages and lymphocytes, immune system cells, the investigators postulate that local production of this neurotoxin may be responsible for central nervous system dysfunction underlying AIDS dementia. They also suggest that monitoring CSF levels of quinolinic acid may serve as a marker for AIDS dementia.

- Intramural investigators have partially purified a peptide fragment derived from the AIDS virus receptor (CD4 molecule) that, when chemically modified, inhibits HIV infectivity in laboratory tests. Discovery of this short chain of 11 amino acids grew out of research on the chemical sequences contained in the CD4 receptor. The substance acts against several variants of the human and Simian AIDS virus and is currently undergoing testing in primates.

- An intramural investigator reports preliminary findings of differences in brain wave responses of seropositive individuals before these individuals show symptoms of AIDS. This suggests a possible test for predicting onset of AIDS.

- NIMH has been involved in the development of therapeutic agents for HIV infection for several years. Uncontrolled, open Phase 1 trials of Peptide T, a protein believed to block the CD4 receptor in the brain, on a small number of AIDS patients demonstrated no adverse effects and some signs of cognitive improvement. Plans are underway fora limited, comparative, controlled trial.

Health Care Worker Training Program - FY 1989

Since FY 1986, NIMH has supported a program to develop model curricula and test methods of providing education and training for health care providers in the neuropsychiatric and psychosocial

aspects of HIV spectrum infection. That program has demonstrated that effective educational techniques result in changes in knowledge, attitudes, and clinical skills. In FY 1989, the NIMH Health Care Worker Program funded four grants to integrate AIDS mental health training into health care AIDS training provided through the HRSA Education and Training Center (ETC) program.

For many health care providers, HIV infection is the first experience with otherwise healthy young people dying. The serious mental disorders that are related to HIV infection, such as dementia and major depression, are challenging our health care provider educational system in new and complex ways. The task has been especially challenging since HIV has affected minority populations disproportionately and stigmatized populations such as gay men and intravenous drug users. The NIMH program has placed special emphasis on reaching health care providers who address the needs of minorities, women, and children.

Other NIMH AIDS Activities - FY 1989

In FY 1989 a number of expert panels and workshop participants were assembled to consider the state of knowledge in key areas and to recommend priorities for future research: (1) neuropsychological assessment in AIDS; (2) neuro-immunology; (3) counseling strategies with HIV testing; (4) anti-gay violence; and (5) depression and suicide related to AIDS.

NIMH convened a group of international experts to develop a battery of measures to assess neuropsychological functioning in HIV-infected individuals. Results include recommendations for a model core assessment battery that includes cognitive and psychiatric measures. NIMH will encourage researchers with federally funded research projects to utilize this battery so that results of research on the neurobehavioral effects of HIV infection can be compared across research sites. With the ability to compare data across a series of research studies and populations, results will provide a larger database for policy decisions, guidance on meeting the health care needs of individuals with neurological impairment, and methods for early detection of the disease. The World Health Organization has asked NIMH to participate in a similar initiative to develop a common measurement battery to be used internationally.

In FY 1989, NIMH sponsored two major meetings on neuro-immunology: one at the University of Pittsburgh in September 1989 focusing on the use of appropriate methodologies in behavioral neuro-immunology research and a second to identify key research needs and promising research strategies.

NIMH convened a group of experts to provide advice concerning the development of a counseling strategy for HIV-positive individuals (and their friends and families) who experience serious psychological reactions to a positive HIV antibody test. The group of experts recommended that counseling and mental health services

for such individuals would be most appropriately provided within an ongoing health service program. Based on their recommendations, the Institute developed a counseling strategy that identifies components of successful HIV counseling programs.

A research workshop on the "Mental Health Aspects of Violence Toward Lesbians and Gay Men: Research Issues and Directions" was held in June 1989. The goal of this workshop was to inform the research community of the state of knowledge and research needs in this area, and to stimulate research proposals to more systematically address the problem.

A meeting was held in October 1989 to assess the state of knowledge regarding depression, suicidal ideation, and suicide attempts/suicides in HIV-infected individuals, and to identify research needs in this area.

In addition, the directors and researchers from the five AIDS Research Centers met to exchange preliminary findings from on-going research projects, share research strategies, and plan collaborative projects. A symposium was presented on minority issues in AIDS research.

Collaborative activities are also underway with CDC in behavior change/prevention initiatives. NIMH is collaborating with several federal agencies including NIH, CDC and the National Institute on Drug Abuse (NIDA) in support of a National Academy of Sciences-National Research Council Committee to advise on behavioral and social AIDS research needs. A series of collaborative activities are also underway with NINDS to advance knowledge about the neuropsychologic, neuropsychiatric, and cognitive sequelae of HIV infection. NIMH also works with the Health Resources and Services Administration in the areas of HIV counseling, health care worker training, and prevention curricula.

Fiscal Year 1990

In FY 1990, NIMH will foster the development of AIDS research with minority populations, adolescents, and the mentally ill. Pediatric AIDS will also be a priority area. Increased emphasis will be placed on the development of theory-based behavioral interventions to prevent or reduce AIDS-related risk behaviors. Research on the central nervous system effects of HIV and HIV-related mental disorders will be expanded. The core neuropsychologic assessment battery will be disseminated to the field and collaborative studies to assess cognitive function across populations will be encouraged.

CNS Effects of HIV

Research will continue on central nervous system effects of HIV, including cognitive and neuropsychologic/neuropsychiatric sequelae; AIDS dementia complex; and development of therapeutic agents for

treatment of HIV infection in the brain. In addition, a series of activities will be undertaken to increase research efforts related to neuropsychological/cognitive deficits and neuro-developmental delays in HIV-infected infants and children. A program announcement planned for FY 1990 will focus on neurological and neuropsychological consequences of HIV infection in infants and children.

Behavioral Immunology/Psycho-neuro-immunology

Research will be continued and expanded to improve understanding of the mechanisms through which behavioral processes affect the immune system and health. The relationship between stress, depression and seropositivity, and their influence on the resistance of the immune system to HIV or opportunistic infections will continue to be supported. Of particular interest are studies involving animal models to assess the role of repeated stressful events on immune function.

Behavior Change/Prevention

In FY 1990, NIMH will continue to place a high priority on AIDS prevention research. The next critical step in the development of a national AIDS prevention strategy requires the design, implementation, and evaluation of population-specific interventions designed to change high-risk, AIDS-related behaviors. These include: therapeutic, (e.g., individual or group), institutional (e.g., schools), and mass-media models. Such an initiative is consistent with recommendations from the National Academy of Sciences and the NIMH AIDS Policy Subcommittee. A multi-site, multi-population research, intervention and evaluation study will be initiated through a cooperative agreement cosponsored by NIDA and NIAAA. Different populations (e.g., Black males, Hispanic females, adolescents, IVDAs, alcohol abusers) will be included. Population-specific measures of constructs contained in major behavior change theories will be developed for each population. This approach will result in a coordinated set of studies across the country aimed at specific population groups.

Natural History and Co-factors

New emphasis will be placed in FY 1990 on psychological and psychiatric consequences of HIV infection (e.g., depression, anxiety, suicidal ideation). Efforts will continue related to the development of measures across research centers and other sites in the following areas: psychiatric and psychosocial assessment, psychosexual assessment, behavior change and prevention, and minority research.

Health Care Worker Program

The NIMH health care provider program will continue to incorporate training of health and mental health personnel in neuropsychiatric and psychosocial aspects of HIV infection/AIDS with the training

programs of the HRSA ETCs. An RFA will be issued in FY 1990 to support additional projects designed to integrate AIDS mental health training with ongoing HRSA ETC efforts. NIMH is also working with the national mental health professional organizations to develop long-term plans for the AIDS training of mental health professionals.

NIMH will evaluate the curricula and materials developed through the NIMH Health Care Worker program to date. Materials deemed highly effective will be disseminated widely.

Other NIMH AIDS Activities - FY 1990

A meeting of the AIDS Research Center Directors and key staff will be held and additional meetings of the research assessment workgroups are planned. A work group on preventive interventions will be initiated in FY 1990 to assess the state of knowledge related to AIDS prevention research and work toward development of effective prevention strategies for populations at risk. The Work Group on Minority Assessment will prepare a report to the Institute. Additional meetings are planned to facilitate collaboration and data sharing among AIDS grantees and AIDS Research Centers. Other research development workshops will focus on AIDS research methodology issues, pediatric AIDS, minority research, adolescents, and the transfer of research findings to clinical settings.

In FY 1990, the NIMH counseling strategy will be made available to federal agencies with a role in HIV counseling and to experts in the field. NIMH will continue to work with CDC and HRSA to refine the counseling strategy and to evaluate ongoing counseling efforts both within CDC counseling and testing programs and within the HRSA AIDS Service Demonstration Projects.

NIMH will continue to encourage research training applications, particularly for the development of minority researchers to investigate important neuroscience and behavioral aspects of AIDS. Training in basic science will be emphasized. Efforts will also be made in FY 1990 to utilize all available mechanisms to foster the development of minority AIDS researchers.

National Institute on Alcohol Abuse and Alcoholism

AIDS

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) supports both extramural and intramural research on AIDS-related issues as well as clinical training to alcoholism treatment providers. Support totaling $6.1 in 1989 included $958 thousand for intramural research and $4.5 million for clinical training programs, extramural research, and support for a new research center on alcohol and immunologic disorders in Tuscon, Arizona.

Extramural Research

The major purpose of the NIAAA AIDS program is to stimulate comprehensive multidisciplinary basic and applied studies to explore the role of alcohol consumption as a potential cofactor in HIV infection and its progression to AIDS. Preliminary research data indicate the dual nature of the relation between alcohol and AIDS. On the psychosocial level, alcohol consumption can result in disinhibition of behaviors, including high risk sexual behaviors, facilitating exposure to HIV infection. On the biological level, alcohol can cause various alterations of the immune system that may compromise host defense against HIV.

Based on these general hypotheses of the role of alcohol as an AIDS cofactor and on the results of several recent studies, NIAAA support is focused on the following research areas.

1. **Epidemiology.** Prospective and cross-sectional studies are supported on the associations between alcohol/drug use and high risk sexual behavior, rates of HIV seroconversion, and the development and clinical course of AIDS. These studies involve various high risk populations, including homosexual and bisexual men and minority groups, in different geographic areas.

2. **Prevention research.** Preliminary data indicate an association between alcohol use and the frequency of engaging in some forms of high risk sexual behavior. Research is being conducted on the role of alcohol in facilitating behaviors which increase the risk of exposure to HIV. These studies might contribute to the development of strategies for prevention of unsafe sexual practices and IV drug use.

3. **Alcohol-induced alterations in immune system.** NIAAA-supported projects target, in particular, those components of immune system which can play a role in facilitating HIV infection or its progression to AIDS. They cover a wide range of basic and clinical immunological research that includes:

- Alcohol and susceptibility to infections. In preliminary studies, alcohol has been shown to facilitate HIV and

tuberculosis infection of some human cells. Alcohol also inhibits activity of one of the blood components (Tumor Necrosis Factor) which may play a role in host defense against opportunistic infections and malignancy. Research along this line will shed light on alcohol's effects on AIDS progression after primary infection.

- Alcohol and immune system development. Recent findings indicate that maternal alcohol consumption has a profound effect on the development of the fetal immune system. Ethanol inhibits transport of antibodies across placenta, suppresses proliferation and maturation of thymocytes, and decreases the offsprings' ability to resist infections. The latter effect has been also shown for paternal alcohol consumption. Further research in this area is needed to clarify the possible role of alcohol as a cofactor of maternal transmission of HIV to fetus and its increased susceptibility to other infections.

- Alcohol and cellular and humoral immunity. Preliminary results have demonstrated inhibiting effects of alcohol both on cellular and humoral components of immune response (on natural killer cells, on function of helper and suppressor T-lymphocytes, and on antibody-secreting B-lymphocytes). Research in this area is crucial in understanding mechanisms of alcohol's effects on host resistance to HIV and opportunistic infections.

- Alcohol and neurohormonal immunomodulation. This is an emerging area of multidisciplinary research on interactions between the nervous, endocrine, and immune systems. Recent preliminary findings indicate that some effects of ethanol on the immune system (lymphocyte functions and some other cell-mediated responses) are associated with neurohormonal changes (corticosteroids, CRF, ACTH, Nerve Growth Factor, norepinephrine). Progress in this new area may contribute to the understanding of immunomodulating effects of alcohol through neuroendocrine regulation.

In addition to the extramural research projects, NIAAA initiated training in AIDS-related alcohol research and has supported collaborative projects to develop and test AIDS and substance abuse curriculums for primary care physicians and alcohol and drug abuse treatment personnel.

Intramural Research

Research on alcohol's role as a cofactor in the etiology of AIDS, and as promoter of opportunistic infection in patients suffering from AIDS, is a major component of the Intramural Research Program. An additional area of AIDS-related research initiated within the Intramural Program is the examination of the effects of the AIDS virus on neuronal function. Current research is focusing on determining the effects of AIDS on the immune system,

and is: investigating the factors controlling T-cell maturation and proliferation; identifying the events that follow binding of the AIDS virus to receptors on lymphocytes; determining the effects of AIDS proteins and related viral coat proteins on neuronal function; and analyzing the mechanisms by which the AIDS viral coat proteins change neuronal metabolism and produce AIDS-related dementia.

Investigations of alcohol's affect on the immune system have enabled the Intramural Program to begin to systematically explore research findings it has developed specifically on the effect of alcohol on lymphocytes. Intramural research scientists working in collaboration with Walter Reed scientists have demonstrated that animals that are chronically treated with alcohol have significantly reduced numbers of lymphocytes in the peripheral blood, spleen, and thymus. Furthermore, the remaining cells in the immune system have diminished ability to divide and proliferate. Significant efforts are now being made to understand how lymphokines control lymphocyte proliferation and how the novel factors for control of T-cell maturation and proliferation have been isolated. These studies will set the stage for detailed analysis of alcohol's mechanism of action.

In addition, Intramural scientists are continuing their efforts in characterizing brain receptor sites that bind the AIDS protein components and on examining alcohol's effect on these brain receptor sites. Completed studies have demonstrated that injection of AIDS proteins and related materials into the brain of animals produces region specific decreases in brain metabolism. The significant decrease in metabolism occurs with extremely small doses of the viral protein and current work is directed at identifying and determining the function of the brain receptors that bind the viral proteins. Work on these receptors is producing insights into how the HIV infection generates dementia in a large portion of AIDS victims.

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HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Maternal and Child Health and Resources Development

ACQUIRED IMMUNE DEFICIENCY SYNDROME

The AIDS functions within the Bureau of Maternal and Child Health and Resources Development include activities relating specifically to development or support of services or resources for the HIV-infected.

Because the epidemiology of HIV differs by geographic area, and cities and communities are at different stages in meeting service needs of infected and at risk populations, grants are provided to areas that have the greatest number of AIDS cases. These funds augment local resources for the needs unique to a particular area with particular emphasis on providing outreach, education, and prevention services for ethnic and minority populations engaging in high-risk behaviors and for IV drug users. By the end of 1989 approximately $50 million had been awarded to 15 states.

Since 1987 grants have been awarded to assist communities in meeting the unique social and medical needs of infants, youth, and women of childbearing age who are HIV-infected or at risk. Among the objectives, the projects are expected to: Demonstrate effective ways to prevent infection, develop coordinated services for infected infants and children, and develop programs to reduce the spread of infection to vulnerable populations of young people.

After FDA approval of Azidothymidine (AZT) in 1987, Congress established the AIDS Drug Reimbursement Program with a $30 million appropriation. Funds are distributed to states based on the number of AIDS patients reported by state as a proportion of the national total. States then reimburse low-income individuals not covered by Medicaid, Medicare, or other insurance. The funds may also be used for any other drugs known to prolong the lives of individuals with AIDS. Thru Fiscal Year 1989 a total of $50 million including $5 million from private industry has been disbursed.

To meet the needs of AIDS and HIV-infected persons, the Bureau manages a grant program designed to assist in renovation or construction of non-acute care facilities for patients. Existing health care systems and facilities were not designed to provide the broad and complicated needs of HIV-infected people resulting in significantly increased demand for both operating and capital costs.

Health Resources and Services Administration
Bureau of Health Professions

Acquired Immune Deficiency Syndrome (AIDS) Activities

Under the Area Health Education Center program, significant emphasis is placed on health professions training, continuing education, and patient education related to HIV/AIDS. A total of $191,050 was awarded among 10 AHEC projects specifically reporting AIDS activities, affecting an estimated 506,810 individuals, including students and population in the areas served by the projects.

Under the section 784 General Internal Medicine/General Pediatrics Residency training program, 18 grantees indicated that approximately 192 residents will benefit from training in the health care needs of the HIV/AIDS infected population. Two faculty development grantees will train 4 faculty in developing and teaching AIDS curriculum; no specific funds were requested for this effort.

An estimated 1,583 trainees under the Physician Assistant Training Program will be exposed to health education in this area by 35 grantees. Eighteen of these programs received a total of $170,663 for their training initiatives. A funding priority to the section 783 program was included in the FY 1989 grant cycle for those projects that demonstrate expansion of current or development and implementation of new curriculum content necessary in caring for HIV infected persons.

The section 786(a) Family Medicine training programs also reported educational interventions in AIDS. Six predoctoral training program grantees and 36 residency training grantees offer didactic and clinical training experiences in treating HIV/AIDS infected persons. Approximately 724 residents will benefit from this training and a total of $38,400 was requested specifically for this purpose. Nine Family Medicine Faculty Development grantees reported faculty training in this area.

Only one Preventive Medicine Residency grantee indicated that it will offer training to one resident in the prevention and treatment of HIV/AIDS in patients.

Nine Podiatric Medicine Primary Care Residency Training Program grantees will emphasize HIV/AIDS education in the training of an estimated 72 podiatry residents. A total of $135,697 was specifically requested for this purpose.

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AIDS Education and Training Centers (ETCs)

The HRSA network of AIDS Education and Training Centers (ETCs) provides: the specialized training needed by existing health care personnel who must care for AIDS patients; the development of model educational programs throughout the continuum of the health professions educational process; and the training of staff in federally supported entities in areas of patient/client counseling and the specific aspects of the delivery of health care to HIV-infected individuals and AIDS patients. The concept of such a program for health professions education and curricula development is in agreement with the recommendations highlighted by both the Presidential Commission report and the Institute of Medicine report.

The current national network of ETCs for health care providers focuses on a principal goal of improving the capacity and capability of the provider community to deliver care to HIV-infected individuals. This activity includes specialized training required by primary health care providers who treat AIDS patients whose conditions vary from cancers or pneumonia to psychosocial problems.

The increase in funding in FY 1990 will attempt to increase the numbers and capabilities of involved health care providers, both for management of early stages of infection as well as the later-stage complications.

Specifically, greater emphasis will be placed on increasing effective training of health care providers on therapeutic advances and studies, targeting training needs in minority communities, extending the developing of faculty training programs in health professional schools, and providing increased training for providers in high risk populations such as community health centers, migrant health centers, sexually transmitted disease clinics, substance abuse programs, and maternal and child health clinics. During the past two years (1988-1989), the ETCs trained over 375,000 health care providers throughout the nation.

In FY 1989, $13,660,052 was awarded to 15 projects, training approximately 221,089 health professionals; in FY 1990 $14,549,000 will continue to support 15 projects, training approximately 400,000 health professionals and in FY 1991, $21,000,000 will support 18 projects, training approximately 800,000 health professionals.

HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Health Care Delivery and Assistance

Community Health Care Services for AIDS

The community health care services for AIDS program concentrates on providing care for persons with the AIDS/HIV infection in community health centers and migrant health centers (C/MHCs) that may ultimately help to relieve the burden on inpatient and long term care public facilities while improving efforts to mainstream the care for this population into the general health care system. These measures are consistent with HRSA's current efforts to mainstream services for the HIV infected into existing primary care networks.

The C/MHCs provide health care to about six million underserved persons in urban and rural settings. While no statistically reliable information is available to estimate the potential number of AIDS/HIV infected patients, it is quite likely that by FY 1993 the number of cumulative cases diagnosed could be 390,000 or higher.

Currently, available services in many communities for persons with AIDS/HIV infection are relatively uncoordinated, fragmented, and often very expensive. Reimbursement for these services is variable and may be inadequate, particularly for out-of-hospital care, since a large and growing number of persons with AIDS are also poor and medically uninsured, or are persons covered only by Medicaid or other forms of public assistance. If a wider range of community oriented, coordinated, ambulatory health care were available, hospital costs and possibly other related costs could be decreased. Focusing resources on outpatient services, home health care, or hospice care is likely to improve continuity and reduce the cost of HIV/AIDS patient care.

In FY 1990 activities will focus on enhancing the capacity of C/MHCs to offer the range of services necessary to impact on the treatment AIDS/HIV disease. During 1990 it estimated that 32,800 people will be served through this program.

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OFFICE OF THE ASSISTANT SECRETARY FOR HEALTH

Office of Minority Health

Acquired Immune Deficiency Syndrome

The Office of Minority Health was established to be the focal point for the implementation of the recommendations contained in the Secretary's Task Force Report on Black and Minority Health and for the formulation and development of policies affecting minority health. The Office works closely with the Public Health Service agencies and other components of the Department to assure that minority health care needs are a priority in Departmental resource allocation decisions.

Since the issuance of the Task Force Report in 1985 and the establishment of the Office of Minority Health, AIDS has also been identified as an excess killer of minorities. The Office, therefore, has a mission regarding AIDS which is similar to the work being done in the six causes of excess deaths identified in the Task Force Report.

Over 50 percent of all AIDS victims are Black or Hispanic. These populations have different risk factors and demographic profiles from the majority population. These differences compounded oftentimes with cultural/language differences require alternative strategies to convey disease prevention information. The Office of Minority Health AIDS activities focus on the following education and prevention efforts:

- Supporting the development of culturally sensitive and culturally appropriate educational materials.

- Conducting technical assistance programs to help minority organizations design, implement and evaluate effective prevention/intervention programs. These efforts include identifying regional technical assistance resources and sponsoring regional technical assistance workshops.

- Assisting minority community-based organizations in the dissemination of AIDS information through the Minority Community Health Coalition Grant Program as well as through the AIDS Education/Prevention Grant Program.

The Minority Community Health Coalition Grant Program provides funding to support innovative community-based disease risk reduction demonstration projects. These grant projects are based on the concept that greater force for change can be achieved by expanding the base of community awareness, support and involvement. This is particularly true if such efforts are carried out by influential community institutions such as

churches, schools and clubs which are organized by recognized community leaders. One or two of these grants awarded each year are targeted to AIDS education and prevention.

The AIDS Education/Prevention Grant Program is a separate grant program created to demonstrate the effectiveness of AIDS/HIV infection education and prevention strategies targeting racial and ethnic minority populations. These grants are awarded to national minority organizations and community-based organizations. These grants expand the range of community-based and national organizations involved in AIDS education/prevention activities and encourage innovative approaches that appropriately address the diversity within and among minority populations.

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INDIAN HEALTH SERVICE

Acquired Immune Deficiency Syndrome (AIDS)

As of August 1989, there were 141 cases of AIDS in American Indians and Alaska Native compared to 105,849 for the general population (CDC HIV/AIDS Surveillance, September 1989). This would produce a cumulative incidence of 8.3 cases per 100,000 population in American Indian and Alaska Natives. This compares to a cumulative incidence of 43.5 cases per 100,000 in United States residents of all other races which yields a risk ratio (RR) of 0.2 for American Indian and Alaska Natives individuals being AIDS cases versus all other races in the U.S.

The Indian Health Service has requested $1,013,000 for the FY 1991 AIDS Program. This represents a $21,000 increase over the FY 1989 budget of $992,000. The IHS plans to spend the funds on epidemiologic studies and surveillance ($95,000), individual and community prevention activities ($650,000), patient care services including ambulatory drug therapy ($268,000). $350,000 of the $1,013,000 will be allocated to the 33 IHS urban Indian programs for prevention activities.

In FY 1991, the IHS will continue its current AIDS prevention and education activities; determine seroprevalence through means of a blinded study; ascertain basic data about knowledge, attitude, and behavior and will assist in funding the early treatment of HIV infected persons.

Background Information:

- In the American Indian and Alaska Native population, the Acquired Immune Deficiency Syndrome (AIDS) is primarily seen primarily in urban areas but is gradually entering the rural and reservation areas.

- In FY 1988 the IHS placed special emphasis on the development of a national AIDS prevention program. The AIDS coordination function was assigned to the Clinical Support Center in Phoenix, and the interagency AIDS liaison function was assigned to the Headquarters Special Initiatives Branch. The IHS sought assistance for its AIDS program from private and government agencies in order to provide a more comprehensive program.

  -- The IHS signed a memorandum of agreement with the Centers for Disease Control (CDC) in FY 1988 to provide funds for the implementation of a prevention program consistent with CDC standards. The IHS received $500,000 and used $350,000 in FY 1988 and $150,000 in FY 1989. To date, over 450 IHS personnel have received HIV Counselor training, and all IHS Health Care Workers have received AIDS prevention education.

-- A memorandum of agreement with the Bureau of Indian Affairs (BIA) in FY 1988 jointly funded several seminars designed to prepare joint IHS-BIA teams to teach AIDS prevention to an estimated 40,000 school children. To date, over 400 BIA teachers, administrators, and school board members have been trained in basic AIDS prevention education. The IHS continues to support AIDS training and education programs for school age children and educators.

-- A memorandum of agreement in FY 1988 with the Administration on Native Americans (ANA) and the Red Cross provided funds and educational materials to support AIDS activities in Urban Indian Projects. The IHS received $60,000 from the ANA.

o For FY 1989, $800,000 was appropriated for the IHS AIDS Program and was used in the following activities: reimbursement of IHS treatment facilities for AIDS drug costs; epidemiology and surveillance; community, tribal government, and school age health education; high risk patient counseling; and health care worker education.

-- $300,000 of the $800,000 was specifically allocated to IHS Urban Indian Programs for AIDS prevention education;

-- $258,000 was used for reservation based prevention programs; and

-- $242,000 was expended for AIDS drugs and AIDS treatment.

o The IHS in cooperation with American Indian and Alaska Native AIDS organizations, CDC and various states have developed 14 Native American AIDS videos, 20 culturally specific pamphlets and over 30 posters dealing with HIV.

o Knowledge, Attitude and Behavior (KAB) surveys have been conducted to determine the level of AIDS awareness of the community. Over twenty (20) surveys have been completed.

o To monitor the spread of the HIV infection, an interagency agreement for $439,000 with CDC's Center for Infectious Disease (CID) in FY 1989 provided funds for IHS conducted tribally approved blinded seroprevalence surveys at selected sites throughout the IHS. At the present time 28 tribes and 2 Urban sites have agreed to be involved in this sera testing. Over 3,000 specimens out of 50,000 projected have been collected. The IHS used $254,865 in 1989, and plans to use the remainder ($184,135) in FY 1990.

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IHS AIDS CURRENT AND FUTURE FUNDING LEVELS

Fiscal Year	Amount	Source	Total
1988	$350,000	CDC	
	$ 60,000	ANA	
	$ 70,000	BIA	$410,000
1989	$800,000	IHS	
	$150,000	CDC	
	$254,865	CDC	
			$1,204,865
1990 (proposed)	$992,000	IHS	
	$184,135	CDC	
	$300,000	CDC	
			$1,476,135
1991 (proposed)	$1,013,000	IHS	$1,013,000

AGENCY FOR HEALTH CARE POLICY AND RESEARCH

Formerly the
National Center for Health Services Research
and Health Care Technology Assessment

ACQUIRED IMMUNODEFICIENCY SYNDROME

The Agency for Health Care Policy and Research (AHCPR) was established on December 19, 1989 as a separate Public Health Service (PHS) agency by the Omnibus Budget Reconciliation Act of 1989, P.L. 101-239. As authorized under a new Title IX of the PHS Act, the purpose of the agency is to enhance the quality, appropriateness, and effectiveness of health care services and to improve access to such services. This goal will be accomplished through the establishment of a broad base of scientific research and through the promotion of improvements in clinical practice and in the organization, financing, and delivery of health care services. The new agency replaces the former National Center for Health Services Research and Health Care Technology Assessment.

As the leader of Federal efforts in outcomes research and health services research, the AHCPR seeks to create and disseminate new knowledge and better understanding of the processes by which health services are made available and how they may be provided more efficiently and effectively. The AHCPR conducts and supports scientific research that tests the assumptions on which current health policies and practices are based, assesses the performance of the health care system, and examines alternate ways to organize, finance, and deliver health services. AHCPR's program is directed towards the needs of health care policymakers, providers, and consumers. It addresses the full array of health care issues, among them AIDS and other illnesses related to the human immunodeficiency virus (HIV).

The set of health services associated with HIV illness is enormous, complex, and changing. It includes preventive services for people at risk of infection, testing and counseling services, outpatient medical and mental health services for those with early symptoms, and a combination of inpatient and outpatient services for persons with AIDS. It involves bringing to bear medical knowledge that is constantly changing, coordinating services provided by a myriad of providers, and bringing into the health care system people who have historically remained outside.

The complexity, urgency, and unique aspects of the HIV epidemic demand a strong program of health services research. Both public and private responses to the epidemic require timely information about how best to plan, create, deliver, organize, finance, and coordinate health care services. Moreover, health services research on HIV illness should be viewed as an essential counterpart to biomedical research; their potential impact is interdependent. For example, two recent developments -- i.e., recommendations by the National Institutes of Health (NIH)

regarding prophylactic drug treatment of persons who are HIV positive but asymptomatic, and the development of new AIDS therapies -expand the patient population and dramatically extend the need for services at both ends of the illness continuum. The implications of such developments, both for costs of care and for a shift toward more chronic care, must be understood and translated into available, accessible services.

The research agenda of the former National Center for Health Services Research and Health Care Technology Assessment (NCHSR) began addressing specific gaps in current knowledge about the HIV epidemic several years ago. These gaps have been identified by a number of groups, including the participants at the Public Health Service (PHS) AIDS Planning Conference held at Charlottesville in June 1988, the Intragovernmental Task Force on AIDS Health Care Delivery, the National Academy of Science's Institute of Medicine, and the Presidential Commission on the Human Immunodeficiency Virus Epidemic. Reports prepared by these groups stress the need for scientific information on the costs, quality, delivery, availability, and financing of services, especially for different risk groups, geographic locations, stage of illness, treatment modalities, and treatment settings. In addition, they emphasize the need for health services research that assesses potential improvements in health care delivery methods, particularly methods to increase the cost effectiveness of care.

The new Agency for Health Care Policy and Research (AHCPR) will continue the work started by NCHSR in addressing the gaps in our knowledge base. Activities addressing HIV illness will be carried out through several programs: extramural research, intramural research, research dissemination and external liaison, and State and Local user liaison. These varied and complementary activities are described in the following pages.

Extramural Research

The Agency's extramural research program has a multi-faceted approach to HIV health services research. The centerpiece of this program is the support of research, through peer-reviewed grants and contracts. In addition, the extramural research program provides extensive technical assistance and policy analysis, facilitates timely dissemination of research findings, and works collaboratively with all concerned to assure that activities are coordinated. These major program elements are described below.

Grant and Contract Research

The extramural research program on AIDS and other HIV illnesses addresses a wide range of issues. An October 1988 program note ("HIV-Related Illnesses: Topics for Health Services Research") identified seven areas as priorities for support. These research priorities are listed and illustrated below. This

list corresponds to the more detailed descriptions of projects, provided later in this report.

1. Cost of Care and Financing Issues

   - o patterns of health service utilization and cost, with special attention to variation by region, risk group, and socioeconomic status
   - o availability and extent of insurance coverage o issues related to the distribution of costs across payers, including the impact of unreimbursed and uncompensated care, and the study of indirect costs

2. Health Status Measures and Information Systems

   - o design of information systems and data banks
   - o development of new measures of severity, functional status, and outcomes
   - o development of simulation models to project AIDS cases and costs

3. Access and Barriers to Care

   - o financial barriers, such as lack of insurance o variations in service availability and use by risk group, severity of illness, and socioeconomic status

4. Quality of Care

   - o patient satisfaction, clinical outcomes
   - o variations by region, treatment setting, and patient characteristics

5. Health Systems Analysis

   - o effects of AIDS on the distribution of health care resources and organization of services
   - o spillover effects and resource tradeoffs, e.g., relationship between AIDS and chronic care

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6. Cost Effectiveness of Alternative Service and Organizational Strategies

   - o centralization vs. decentralization of AIDS beds within hospitals
   - o role and effectiveness of volunteer services

7. Provider Issues

   - o training, attitudes, and willingness to provide services to AIDS patients
   - o stress and burnout
   - o choice of specialty, location, and other practice decisions

As a set, the Agency's research projects are beginning to provide information from many States, different regions of the country, and from areas with high and low AIDS prevalence. They will provide information about persons in all high risk groups and socioeconomic circumstances, about the full spectrum of HIV illness (i.e., from asymptomatic to overt AIDS), and about a wide range of inpatient and outpatient settings. The portfolio includes both large and small projects, some of which provide in-depth information pertinent to one priority area and some of which address several priority areas.

Cost of Care and Financing Issues

"AIDS Cost and Service Utilization Survey" (ACSUS) Westat, Inc., Rockville, MD, Contract No. 282-89-0020

ACSUS is a national survey to collect uniform data on the utilization and costs of health and social services for parsons with AIDS and other HIV-related illnesses. Interviews will be conducted every 3 months over an 18-month period, with a sample of approximately 1900 adults and adolescents plus 100 children. In addition to medical care, respondents will be asked about their use of social, mental health, and oral health services, informal social supports, barriers to care, employment history, and quality of life. Interview data will be supplemented by information abstracted from patient records and information supplied by providers and insurers.

These sources will provide a comprehensive picture of the direct and indirect costs of medical and support services, during various stages of HIV-related illness. Data will include third-party and out-of-pocket payments,

for both inpatient and outpatient care, including care received in physicians' offices, ambulatory clinics, and the patient's home. Utilization and charges for the services of physicians, nurses, and other health care workers will be obtained, as will charges for drugs, medical supplies, and devices.

Final products of the contract will include documented data tapes for use by the research community. In addition, ACSUS data will enhance AHCPR's capacity to provide timely input to policy questions. The data will support examination of utilization, cost, and access across HIV exposure categories (e.g., homosexual, heterosexual, or intravenous drug use), stage of illness, demographic characteristics, geographic area, and payment source. By addressing the full spectrum of HIV-related illness and the range of health care providers and payers, ACSUS will provide a rich source of data for research and the basis for policy-relevant analyses concerning the utilization and costs of health care services associated with HIV illness.

Andrulis, Dennis P.; National Public Health and Hospitals Institute, "1987 U.S. Hospital AIDS Survey," Grant No. HS06129

A survey conducted in over 600 hospitals will assess the financial and programmatic impact of AIDS on U.S. hospitals and will permit comparisons with 1985 data. Variables include demographic characteristics of the patient populations, financing of care, and types of services provided. The 1987 data include a survey of pediatric cases and a study of costs related to the use of AZT. Analysis will focus on differences due to geographic location and hospital type, as well as changes over time.

Crystal, Stephen; Rutgers University "Health Care Costs and Utilization in AIDS Home Care," Grant No. HS06339

This is an in-depth study of the utilization and costs of health and social services for participants in New Jersey's Home and Community-based Services Waiver for Persons with AIDS/ARC -- i.e., the AIDS Community Care Alternatives Program (ACCAP). Data sources include complete Medicaid payment records for all program enrolles, case management records, and personal interviews conducted monthly with 400 new enrolles, for up to 18 months. A combination of cross-sectional and longitudinal analyses will focus on service utilization across subgroups of persons with AIDS-related illnesses, including ethnic minorities, women, and children; the interrelationships among home care, institutional care, and social supports; and differences in utilization and costs for persons who are, and those who are not, enrolled in ACCAP.

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Epstein, Arnold M., Harvard U. School of Public Health, "Costs, Correlates and Outcomes for Persons with AIDS," Grant No. HS06239

Investigators will collect and analyze information on the use and costs of medical services and outcomes for a cohort of approximately 500 AIDS patients who receive primary care at one of three Boston-area providers. Data will include the costs of a wide range of inpatient and outpatient services, as well as indirect costs associated with disability and premature mortality. Data on patient clinical characteristics, stage of illness, functional status, and socioeconomic status will be used to explain costs and to predict costs, utilization, functioning, satisfaction, and survival.

Hidalgo, Julia; Dept. of Health and Mental Hygiene, State of Maryland, "Cost of Treatment of IV Drug Users with AIDS," Grant No. HS06185

Using a Statewide (Maryland) AIDS information system, this study will identify characteristics of intravenous drug abusers with AIDS, study the use and costs of health care services they receive, the fiscal impact of their care on Medicaid and other public programs, and the level of uncompensated hospital costs. Results will be useful for researchers, policy makers, and other States developing AIDS information systems.

Hogan, Andrew J.; Michigan State University, "Costs of Health Services for HIV Infected Individuals," Grant No. HS06260

Using Medicaid records and some private health insurance data, this project will study use and cost of services for HIV-related illnesses between January 1984 and March 1989 in Michigan. Hypotheses focus on differences in use and cost by risk group and sex, on the impact of AZT on average monthly Medicaid payments, and on apparent underutilization of services by some Aids patients.

Pascal, Anthony H.; Rand Corp., "Financing Treatment Costs for IVDA AIDS Patients," Grant No. HS06130

Based on a random sample of AIDS patients affiliated with one New York City hospital, data will be collected to assess the cost burden of treatment for a panel of 50 intravenous drug abusers. Data on costs, payments, patient economic variables, and service utilization will be used to construct longitudinal profiles of these patients.

Schwartz, Rachel; National Perinatal Information Center, "Pediatric AIDS: Local Responses, Service Use, and Cost," Grant No. HS06271

This project will provide both longitudinal and cross-sectional data about the utilization and costs of inpatient and outpatient care for infants, children, and women with AIDS. One aspect focuses on discharge, billing, and cost data from 10 hospitals in 5 urban areas with high incidence of pediatric AIDS and will analyze trends from 1987 to 1991. In addition, detailed case studies will be developed to address questions about alternate community responses to meeting the health care needs of women and children with AIDS and to obtain information on outpatient services.

Seage, George R.; Boston Dept. of Health and Hospitals, "Variation in Cost of AIDS Related to Gender and Risk Status," Grant No. HS06150

This study will obtain data for the State of Massachusetts on the cost and utilization of inpatient services by all women and intravenous drug users diagnosed with AIDS from January 1987 to January 1989. Estimates will be made of costs per patient, controlling for stage of disease, site of hospitalization, socioeconomic status, and levels of social support. These data will be compared with data for a sample of male homosexuals/ bisexuals diagnosed during the same period.

Scitovsky, Anne A.; Palo Alto Medical Foundation/Research Institute, "AIDS Research Protocols," Contract No. 282-87-0050

This contract developed six research protocols focused on substantive and methodological issues in AIDS health services research, to assist investigators in developing proposals and research plans. The project was instrumental in the development of the scope of work for, and in planning for the cooperation of provider sites in, the current ACSUS contract. The protocols, available through AHCPR's Publications and Information Branch, are entitled:

No. 1: "Estimating the Use and Cost of Medical, Social, and Support Services for Persons with AIDS and ARC"

No.2: "Comparisons of the Cost Effectiveness of Various Treatment Modalities"

No.3: "Comparisons of the Cost Effectiveness of Alternative Models for Organizing Services for Persons with AIDS"

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No.4: "Comparing the Cost of AIDS to the Cost of Other Illnesses"

No.5: "Estimating the Demand, Supply, and National Costs of HIV Testing"

No.6: "HIV-Related Training Needs, Programs, and Costs"

Paringer, Lynn; Western Consortium for Public Health, "Determinants of Individual Demand for HIV Testing," Grant No. HS06352

This study will identify the factors influencing demand for voluntary HIV testing and develop a model to predict future demand. Data to be analyzed are from the "AIDS Knowledge and Attitudes" supplement to the National Center for Health Statistics' National Interview Survey for 1987 and 1988. In addition, available data on the policies of individual States regarding testing and confidentiality will be incorporated. Separate regression models will be estimated for the two years of data, and some comparisons will be drawn. The analysis will provide: (1) historical view of demand for HIV testing (i.e., prior to effective treatment); (2) estimates of demand among different subpopulations: (3) impact of AIDS knowledge on demand; and (4) impact of State policies on demand.

Health Status Measures and Information Systems

Fries, James J.; Stanford University Medical School, "ATHOS -- AIDS Time-Oriented Health Outcome Study," Grant No. HS06211

This study will develop a prospective, longitudinal information system on 5,000 to 8,000 AIDS, ARC, HIV--positive, and at-risk subjects in California. Clinical, laboratory, economic, and quality of life data will be obtained from 5 private practices and 5 indigent clinics. Analyses will include: factors influencing transition between clinical states, quality of life, patient outcome, and costs; as well as assessment of both direct and indirect costs and efficacy of both approved and unapproved therapies.

Hay, Joel W.; The Hoover Institution, Stanford University, "Projecting the Costs of AIDS/ARC in the United States," Grant No. HS06092

The objective of this research is to develop a model for projecting costs related to AIDS and ARC that can be easily modified as new epidemiological information and treatments become available. Using the Medi-Cal AIDS

patient database and data for two other regions, the researchers will refine and validate results of an earlier study. The model will permit estimation of lifetime costs per patient based on medical diagnosis and treatment decision tree algorithms.

Pagano, Marcello; Harvard U. School of Public Health "Modeling Methodology for Projecting the AIDS Epidemic," Grant No. HS06183

The researchers will develop a statistical simulation model for studying the progression and spread of AIDS, to permit predictions of the epidemic's future course and to assess the impact of potential interventions. Based on express time transitions as a stochastic progression, the model will incorporate uncertainty about model parameters.

Payne, Susan McNair Cobb; Boston University "Validating Hospital Discharge and AIDS Surveillance Data," Grant No. HS06426

This study will investigate the feasibility of using routinely collected hospital discharge data from Boston's Uniform Hospital Discharge Data Set to track hospital utilization and charges for patients with AIDS. Patients and their patterns of hospital utilization and charges will be described. By cross-validating these data with surveillance data, the investigators will assess the completeness of AIDS case reporting.

Sechrest, Lee; University of Arizona, "Health Services Research Methodology: A Focus on AIDS," Grant No. HS05306

This conference, held in June 1988 in Tucson, Arizona, highlighted alternative research designs, data collection methods, and statistical techniques suitable for AIDS health services research. Proceedings of the conference, published by NCHSR, include eight feature articles and comments on each. The publication is available from the National Technical Information Service, accession no. PB90-100074/AS.

Williams, Sankey V.; University of Pennsylvania, "Developing Tools to Study Resource Consumption in AIDS," Grant No. HS06230

This pilot project will develop methods that use computerized hospital data-reporting systems to identify AIDS patients and improve understanding of the costs of care and patterns of inpatient resource use for AIDS patients. Discharge data from Philadelphia's five medical school teaching hospitals will be studied for a 30-month period. Resource consumption patterns within and between hospitals will be compared.

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Access and Barriers to Care

Blendon, Robert Jay; Harvard U. School of Public Health, "Discriminatory Attitudes and Knowledge about AIDS," Grant No. HS06379

This is a secondary analysis of public opinion survey data to examine the relationship between hostile attitudes toward persons who are infected with HIV and misinformation about how the virus is transmitted. Data come from surveys conducted by the Roper Center for Public Opinion Research, the Gallup Organization, and the Los Angeles Times, among randomly selected, national household samples, since 1985. Variables include knowledge and beliefs about how HIV is transmitted, demographic characteristics, attitudes, and moral judgments about persons who are infected. Findings will inform the policy debate regarding the need for antidiscrimination legislation to protect individuals infected with HIV.

Fleishman, John A.; Brown University, "Delivery of Home Care for People with AIDS," Grant No. HS06378

This grant will obtain information about the availability and organization of home health services for people with AIDS. Data will be collected from a sample of eight home health care agencies, providing different levels of service to persons with AIDS, in nine cities with varying incidence of AIDS. Issues to be addressed are: 1) organizational characteristics of agencies that provide various amounts of care to AIDS patients; 2) organization of AIDS services within these agencies; 3) coordination with other service providers; and 4) problems in delivering home care to AIDS patients. Analysis will include both descriptive statistics and formulation of multivariate models to help explain home care agencies' involvement with the AIDS population.

Kane, Rosalie; University of Minnesota, "Prospects for Caring for Persons with AIDS in Nursing Homes: Perspectives of Current Residents, Policy Implications," Contract No. 282-87-0049, Task Item No. 35

This project will explore the issues surrounding admission of persons with AIDS to nursing homes in Minnesota. The researchers will interview key informants and conduct a series of focus groups with nursing home residents. The report will address policy implications, including quality and cost of care, and lay out a research agenda related to AIDS care in nursing homes.

Kass, Nancy E.; Johns Hopkins University, "AIDS and Insurance: The Experience of a High-Risk Cohort," Grant No. HS06108

This is a dissertation grant to survey gay and bisexual men who voluntarily participate in the Baltimore and Los Angeles chapters of the NIH-funded Multicenter AIDS Cohort Study. The research addresses issues of access to insurance by examining the relationships of HIV testing, antibody status, and symptom status to the experiences of respondents in applying for health, life, or disability insurance over the past five years, and their current insurance coverage.

Quality of Care

Avorn, Jerome; Beth Israel Hospital, "Improving the Accuracy of Transfusion Decisionmaking," Grant No. HS05300

This is a multicenter, randomized, controlled trial of an educational intervention designed to improve the cost effectiveness and clinical appropriateness of blood product utilization. It measures the effect of the intervention on the use of blood products and identifies patient and physician characteristics that enhance or impede this effect. Clinical appropriateness is defined in terms of reduced risk of transmitting diseases, including hepatitis and AIDS.

Kanouse, David E.; The Rand Corp., "The Quality of Care in AIDS: Pneumocystis Carinii Pneumonia," Grant No. HS06016

This project will examine the impact of patient characteristics, disease, and processes of care on clinical outcomes for AIDS patients and develop predictors of clinical outcomes. Data are based on hospital records of 600 newly diagnosed AIDS patients in Southern California with an initial episode of pneumocystis carinii pneumonia.

Lo, Bernard; University of California at San Francisco, "Variability in 'No Code' Orders Among Very Ill Patients," Grant No. HS05791

This completed study examined whether decisions to write "Do Not Resuscitate" (DNR) orders are made equitably for patients with different life-threatening illnesses. Retrospective data were collected at three teaching hospitals for patients with a diagnosis of AIDS, non-resectable non-small cell lung cancer, cirrhosis with esophageal varices, or severe congestive heart failure with coronary artery disease. Significantly higher rates of DNR orders were found for patients with AIDS and cancer, and these could not be explained by severity of illness,

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functional and mental status, or reason for hospitalization. Some variation between diagnostic groups can be explained by physician differences in: attitude and approach to patients, interpretation of prognostic data, and perceptions of quality of life associated with each disease. The investigators suggest that physicians approach the issue of DNR orders differently across disease categories for patients with comparable prognoses. They conclude that decisions about resuscitation ought to be made with more attention to patient preference.

Stoeckle, John D.; Massachusetts General Hospital, "Living Wills: For Primary Care, AIDS, and Cancer Patients," Grant No. HS06120

Patients seen in primary care physician practices, patients with AIDS, and patients on a telephone registry will be interviewed to obtain information about the "durability" of their positions on living wills. Descriptive and analytic information will be used to tailor pre-drafted living will forms to better meet the needs of patients whose situation and treatment preferences might change. Preliminary findings suggest that discussions about treatment options in physicians' offices enable patients to make specific choices and may later improve adherence to those choices.

Zussman, Robert; Columbia University, "AIDS and Other Patients' Use of ICU Technologies," Grant No. HS05548

This is an ethnographic investigation exploring data from intensive care units (ICUs) in two States. The principal aim is to examine the ways in which decisions are made to use elaborate and expensive medical technologies. The study will focus on the process by which decisions are made and on their outcomes, with attention to the treatment of patients (including several with diagnosed HIV infection) who pose difficult social and ethical problems.

Health Systems Analysis

Lambright, W. Henry; Syracuse Research Corp., "The New York State Response to AIDS," Grant No. HS06184

New York State's emergency response to AIDS, especially the work of the AIDS Institute, will be studied. The focus will be on the coordinating role of the Institute and its regional outreach organizations. By identifying factors that have led to success and to problems in coping with AIDS in New York, the investigators will define a model administrative organization that other States may replicate.

Cost Effectiveness of Alternative Service and Organizational Strategies

Keenan, Joseph M.; University of Minnesota, "Research Agenda on the Community-Based Care of Persons with AIDS," Grant No. HS06224

This grant supported a conference on research problems and issues related to home and community-based care for AIDS patients. The purpose of the conference was to identify and prioritize research issues related to appropriate care settings, quality of care, cost, health care policy, and both lay and professional caregivers. The conference met in Minneapolis, August 14-16, 1989.

Mor, Vincent; Brown University, "Longitudinal Study of AIDS Health Services Use and Costs," Grant No. HS06214

This project will build upon an evaluation of the Robert Wood Johnson Foundation's AIDS Health Services Demonstration by reinterviewing 1,224 patients from 9 to 12 months after their initial evaluation interview. Hospital, clinic, physician, and home care service use records will also be abstracted. The overall goal is to describe patterns of medical and social service use by persons with AIDS, to determine the degree to which their needs are met, and the degree to which their preferences for palliative versus aggressive treatment alter as their disease progresses.

Scitovsky, Anne A.; Palo Alto Medical Foundation/Research Institute, "Medical Care Costs of AIDS Patients in San Francisco," Grant No. HS05916

This study prospectively examined treatment and cost variations for AIDS patients in the San Francisco area. Comparisons were made among patients receiving care in a public hospital, an HMO, and from physicians in the community. Those treated at the community hospital had higher inpatient utilization and higher costs than patients in the other settings. Patients of community physicians had the highest utilization of counseling services. Overall, outpatient care accounted for approximately 30 percent of total personal medical expenditures, a larger share than found in previous studies.

Sowell, Richard L.; Medical College of Georgia, "The Effect of Case Management on Cost of Care for PWAs," Grant No. HS06315

This study will compare the cost of two alternative approaches to delivery of health care to persons with AIDS. The subjects are men, ages 20 through 49, who died of AIDS,

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in Georgia, between 1986 and 1989. A case management approach will be compared with a less organized, ad hoc approach to care, in terms of lifetime costs. Data will be drawn from medical and financial records at four hospitals throughout Georgia.

Provider Issues

Colombotos, John; Columbia University, "Physicians, Nurses, and AIDS: A National Study," Grant No. HS06359

The researchers will conduct a national survey of physicians and nurses to obtain data on how their knowledge, attitudes, risk perceptions, practices, and career plans relate to AIDS. Descriptive findings will be extended through analysis of the interrelationships among these variables, e.g., the relationship between knowledge about AIDS and willingness to treat AIDS patients. Variations associated with respondents' professional characteristics and personal background will be studied. Other analyses will focus on the influence of geographic location, comparing health care workers from San Francisco with those from New York/New Jersey, and examining the possible influence on health care workers of the cumulative AIDS caseload in their State.

Kelly, Joyce V.; Association of American Medical Colleges, "AIDS and Medical Residency Selection in New York, San Francisco, and Los Angeles," Grant No. HS06428

This project will examine the effects of the AIDS epidemic on the selection of post-graduate training by senior medical students in three cities with very high AIDS caseloads. Available data on medical students, residency programs, and residency matches will be linked with measures of the prevalence of AIDS in residency hospitals, to create a new database for this and future studies. Specialty choice and preferred hospital location will be analyzed in terms of student background, exposure to AIDS in medical school, student test scores, and characteristics of the residency programs. Trends between 1983 and 1988 will be examined.

Publications on HIV Illness by Extramural Research Staff

- Hellinger, Fred. "Updated Forecasts of the Medical Care Costs of AIDS: 1989-1993", forthcoming in the January/February 1990 issue of Public Health Reports.

- Hellinger, Fred. "National Forecasts of the Medical Care Costs of Acquired Immunodeficiency Syndrome: 1988-1992", Inquiry, Volume 25, Number 4, Winter 1988, pp. 469-484.

- Hellinger, Fred. "Forecasting the Personal Medical Care Costs of Acquired Immunodeficiency Syndrome from 1988 through 1991", Public Health Reports, Volume 103, Number 3, May/June 1988, pp. 309-319; and reprinted in Financing Care for Persons with AIDS: The First Studies, 1985-1988, edited by Daniel M. Fox and Emily H. Thomas, University Publishing Group, Frederick, Maryland, forthcoming.

Intramural Research

The Hospital Studies Program (HSP) is one of three major areas of policy research and analysis in AHCPR's intramural research program. The HSP focuses on questions relating to the delivery of health care in short-term general hospitals in the United States. The various research studies undertaken by this program depend on two very large data bases that have been developed over the past decade to facilitate hospital-related policy research.

The first data base, the Hospital Cost and Utilization Project (HCUP), contains information on a sample of more than 400 hospitals. Included are more than 55 million summary abstracts of all patient discharges during two time periods, 1970-77 and 1980-87, characteristics of the institutions and the markets in which they operate, and background of the medical staff.

The second large data base, the State Hospital Data Project (SHDP), contains data on almost 15 million discharges from acute care hospitals in Maryland, New York, and Massachusetts from 1983 to the present and on the characteristics of those facilities.

Because of their size, these data bases provide the means to study even very rare medical events. Both the HCUP and SHDP data sets are being employed to study patients hospitalized for AIDS. For example, the relatively large number of AIDS cases included in the New York State data has provided the clinical information used to stage hospitalized AIDS patients by severity of illness. Such staging is essential to studies that compare different therapeutic approaches to treating AIDS patients or to compare costs of treatment across different hospitals and regions of the country. Both HCUP and SHDP data have been used to examine the costs and financing of inpatient care for AIDS taking into account differences in patient severity. These data will be used in future studies of the epidemiology of AIDS, the variations in patterns of hospital treatments, and the factors responsible for differences between hospitals and regions with respect to the cost of diagnosis and treatment.

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Intramural Research on AIDS from the Hospital Cost and Utilization Project:

Ball, Judy K., Joyce V. Kelly, and Barbara J. Turner. "Third-Party Financing for AIDS Hospitalizations in New York." Presented at the IV International Conference on AIDS, Stockholm, Sweden, June 12-16, 1988. Currently under review for publication.

Using data from nearly 6000 AIDS discharges from all hospitals in Greater New York in 1985, this study found that financing for AIDS hospitalizations was shared almost equally by public and private payors and the bulk of AIDS inpatient care was provided in private teaching hospitals. AIDS patients had longer stays in public hospitals compared to private facilities, had shorter stays if they were "self pay" patients compared to Blue Cross patients, and had similar lengths of stay if they were Medicaid patients compared to Blue Cross patients, after controlling for source of care.

Thaul, Susan and Judy K. Ball, "Pediatric HIV-Related Discharges in a Sample of U.S. Hospitals: Demographics, Diagnoses, and Resource Use," presented at the V International Conference on AIDS, Montreal, Canada, June 5-9, 1989. Currently undergoing revisions for journal submission.

This paper describes the inpatient care provided to children with AIDS in non-specialty U.S. hospitals, based on 196 pediatric discharges with AIDS-related diagnoses in 1986-87 from the Hospital Cost and Utilization Project (HCUP). Pediatric AIDS discharges are compared with 10,538 adult AIDS discharges and with a sample of 32,166 pediatric discharges for any diagnosis. Pediatric AIDS hospitalizations are more likely to be government financed, longer, and more expensive than all-cause pediatric stays. Compared to adult AIDS, pediatric AIDS discharges are again more likely to be government financed. Although their lengths of stay and charges are not significantly different when using common averages, pediatric stays are significantly shorter than adult stays based on a comparison of geometric means, which minimizes the effect of extraordinarily long stays.

Turner, Barbara J. and Judy K. Ball, "The Impact of Non-opportunistic Infections on Mortality in a National Sample of AIDS Hospitalizations," presented at the V International Conference on AIDS, Montreal, Canada, June 5-9, 1989. Currently undergoing revisions for journal submission.

This study estimates the relative effects of nonopportunistic infections (NOI), opportunistic infections

(OI), and other clinical conditions on the odds of surviving an acute inpatient episode, controlling for patient demographic characteristics, the hospital's AIDS experience, and region of the U.S. Among the opportunistic organisms, which occurred in 56% of hospitalizations, Pneumocystis carinii pneumonia, cryptococcosis, and non-tuberculous mycobacterial infections were associated with the highest risks of inpatient death. Among non-opportunistic infections, which occurred in 38% of AIDS hospitalizations, those involving the lung or those that were disseminated also significantly increased the likelihood of inpatient death.

Intramural Research on AIDS from the State Hospital Data Project:

Ball, Judy K. and Barbara J. Turner, "Distribution and Characteristics of AIDS Hospitalizations in the U.S., 1986-87," presented at the V International Conference on AIDS, Montreal, Canada, June 5-9, 1989. Currently undergoing revisions for AHCPR publication.

Using data on more than 10,500 adult AIDS discharges in 1986-87 from a national sample of hospitals, this study explores sources of care and variations in resource use and financing for AIDS inpatient care across geographic regions of the U.S. Inpatient care for AIDS was concentrated in urban areas and in facilities that were larger than average, were controlled by private not-for-profit organizations, and had teaching programs. On average, lengths of stay and total charges were highest in New York, but charge per day, a measure of service intensity, was highest in California. Private insurance was the expected payor for more than more than 40% of discharges, regardless of geographic region, while the rate of uninsured discharges was highest in the south where Medicaid eligibility is more restrictive.

Kelly, Joyce V., Judy K. Ball, and Barbara J. Turner, "Duration and Costs of AIDS Hospitalizations in New York: Variations by Patient Severity of Illness and Hospital Type," forthcoming in Medical Care.

The study analyzes hospital resource use by AIDS patients with a multivariate model that incorporates hospital characteristics, patient demographic characteristics, and severity of illness. More severely ill AIDS patients were found to have considerably longer stays and higher total charges, regardless of hospital type. Moreover, severity of illness proved to be a powerful predictor, accounting for most of the variation explained in length of stay and charges.

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Turner, Barbara J., Joyce V. Kelly, and Judy K. Ball, "A Severity Classification System for AIDS Hospitalizations," Medical Care, v. 27, no. 4, April 1989.

This paper describes the development of a new model for classifying hospitalized patients with AIDS according to their severity of illness. The project began with a clinical model of AIDS severity, based on the clinical literature and expert opinion. Then, the clinical model was tested empirically using data on more than 6000 AIDS hospitalization in New York in 1985. The final classification system has 20 substages, grouped into three stages, with inpatient mortality rates increasing from 6% to 60%. A computerized version of the system is available from the National Technical Information Service (Order numbers: PB88-249404,PB88-249396, PB88-249412).

Other intramural research on AIDS:

Kelly, Joyce V. and Judy K. Ball, Selected Bibliography on AIDS for Health Services Research, Publication No. NCHSR 87-36, September 1987.

The first in what has become an annual series, this bibliography provides health services researchers with more than 300 annotated citations for articles related to AIDS service delivery issues.

Rizzo, John A., William D. Marder, and Richard J. Willke, "Physician Contact with and Attitudes toward HIV Seropositive Patients: Results from a National Survey," forthcoming in Medical Care.

This paper presents the first national estimates of physician involvement in and attitudes toward the treatment of HIV-positive patients, using data from a nationally representative sample of non-federal patient care physicians surveyed in 1988 by the American Medical Association. Nearly half of the survey respondents treated at least one HIV-positive patient, with an average of 6.7 HIV-positive patients per physician. Although perceived responsibility to treat HIV positives was uniformly quite strong across physician specialties, years of experience, and practice types, there were pronounced differences in actual physician involvement along these same dimensions.

Turner, Barbara J. and Judy K. Ball, "AIDS Severity of Illness Classification Systems," in William N. LeVee (ed.), New Perspectives on HIV-Related Illnesses: Progress in Health Services Research, Publication No. (PHS) 89-3449, September 1989.

This paper reviews existing methods of measuring the severity of illness of AIDS patients. Particular attention is given to two recent advances in AIDS severity measurement: the development and application of a Severity Classification for AIDS Hospitalizations (SCAH) and current efforts to create a Severity Index for AIDS Patients (SIAP) which will incorporate longitudinal data about an AIDS patient's disease experience as well as vital patient demographic information.

Turner, Barbara J., Judy K. Ball, and Thomas R. Fanning, "Severity Classification Systems for AIDS: Implications for Research on Community-Based Care," forthcoming in Proceedings of Community-Based Care of Persons with AIDS: Developing a Research Agenda.

This paper discusses the importance of severity of illness measurement to health services research on AIDS and HIV infection. It reviews the most commonly used severity classifications for AIDS and HIV infection, including recent advances in AIDS severity measurement that exploit rich secondary data sources, and proposes several new directions for AIDS health services research that relate to community-based settings of care.

User Liaison Program

The User Liaison Program was established to convey relevant and timely health services research findings and related information to State and local government policymakers in a manner that allows such officials to absorb this information and thus heighten the possibility of research being employed in the decision making process. One of the major goals of the Program is to identify pressing informational needs of State and local government officials that could be addressed by new health services research studies or by syntheses of existing research findings.

During FY 1989, the User Liaison Program conducted the seventh in a series of workshops dealing with the impact of the AIDS/HIV epidemic on State governments. The subjects addressed over a three and one-half day period included: basic information regarding the disease; the transmission of the AIDS virus; testing and counseling issues; financing of health care for AIDS patients; costs of treating AIDS patients; legal issues; the impact of AIDS on minority groups, as well as children; and the particular patterns of the spread of AIDS in the drug user community.

In addition to these subjects, the workshop took place four days after the announcement from the National Institutes of Health that AZT treatment for sero-positive individuals with low

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T-cell counts would delay the onset of the disease. Fortunately, an official from the National Institute of Allergy and Infectious Diseases (NIAID) was present at the workshop as a resource person and was able to provide the participants with the pertinent scientific data regarding that dramatic announcement. Other presenters addressed the financial implications of this announcement for States. The workshop audience included State legislators, senior legislative staff and State Medicaid officials.

Technical Assistance and Policy Analysis

AHCPR (formerly NCHSR) staff provide technical assistance to Federal and local governments, the research community, health care providers, and the public. Examples of significant activities include:

- Development of briefing information and analysis of the costs of drug reimbursement policy, costs of prophylactic drug treatment for HIV patients, survival estimates for AIDS patients, and cost of illness comparisons for use by the National AIDS Program Office (NAPO);

- Assistance to the Department of Defense in the design of research on the effectiveness of the organization of health services for HIV positive military personnel and their dependents;

- Assistance to the Centers for Disease Control (CDC) regarding estimates of the number of AIDS patients and related hospitalizations;

- Technical review and consultation on the evaluation of AIDS Service Demonstration Projects, sponsored by the Health Resources and Services Administration (HRSA);

- At the request of members of Congress, provision of information regarding trade-offs between mental health services and AIDS care within mental health and drug treatment settings; detailed documentation of the NCHSR research program on HIV illness;

- Assistance to the State of California legislature regarding the review of a report on the costs of AIDS care; and,

- Review of proposed manuscripts on HIV illness for the Journal of the American Medical Association, Milbank Quarterly, Health Care Finance Review, and Public Health Reports.

Dissemination/Conferences/Publications

In recognition of the importance of rapid dissemination of research findings on HIV illness, AHCPR (formerly NCHSR) has sponsored or cosponsored three conferences on HIV research, seven workshops on the impact of the AIDS/HIV epidemic on State governments, participated in numerous other professional meetings, and developed publications useful to policy, research, and clinical decisionmaking. The following examples are provided:

- "Health Services Research Methodology: A Focus on AIDS," held in Tucson in June 1988. This conference was supported by grant HS05306. Conference proceedings have been published (see below).

- "New Perspectives on HIV-Related Illnesses: Progress in Health Services Research." Sponsored in cooperation with the Health Care Financing Administration, this conference was held in Miami in May 1989. Sessions focused on recent health services research on the cost and financing of HIV care, forecasting and measurement, and health systems issues. Presenters, all recognized experts, included representatives of the CDC, HRSA, and NAPO, as well as NCHSR grantees. Papers were on display at the Fifth International Conference on AIDS, in Montreal. Conference proceedings have been published (see below).

- "Community-Based Care for Persons with AIDS: Developing a Research Agenda." This conference was held in Minneapolis in August 1989. It was supported by grant HS06224 with assistance from HRSA. Proceedings are in press.

Other HIV conferences and meetings in which AHCPR staff have participated in planning and/or as presenters:

- Sessions with State and local representatives focusing on HIV-related research and policy;

- Second Annual AIDS Conference sponsored by the San Francisco Department of Health, San Francisco, October 1, 1988, on forecasting the costs of AIDS;

- Annual meeting of the American Public Health Association in Boston, October 1988, on the costs of AIDS;

- Fifth International AIDS Conference, Montreal, Canada, June 1989, on forecasting the medical care costs of AIDS for 1989-1993;

- National Minority Conference on HIV-Related Illnesses, Washington D.C., August 1989;

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- CDC-sponsored HIV/AIDS Projections Meeting, Atlanta, October 1989;

- Annual meeting of the American Public Health Association workshop on methodological issues in AIDS health services research, Chicago, October 1989;

- Association of Medical Education and Research in Substance Abuse meeting on research priorities in the study of primary health care for HIV-positive substance abusers, Rockville, MD, November 1989;

- National AIDS Network Conference workshop on community-based organizations and HIV-related research, Washington D.C., November 1989;

- Pan American Health Organization Conference on AIDS, Santo Domingo, Dominican Republic, November 1989; and

- NCHSR co-sponsored, with nine other PHS agencies/offices, the National Conference on HIV Infection and AIDS Among Racial and Ethnic Populations. NCHSR staff served on the executive planning committee for this conference, and co-chaired a subcommittee that developed panels and workshops on financing and funding AIDS education, treatment, and research programs. This conference was targeted at front line community based organizations that provide services to minorities and ethnic populations, who are disproportionately affected by HIV infections and AIDS.

NCHSR publications on HIV illness:

- Selected Bibliography on AIDS for Health Services Research, published September 1987, revised September 1988, and 1989. (NTIS accession no. for 1989 edition is PB 90-101064)

- Conference proceedings, Health Services Research Methodology: A Focus on AIDS. (NTIS accession no. PB 90-100074/AS)

- Conference proceedings, New Perspectives on HIV-Related Illnesses: Progress in Health Services Research. (NTIS accession no. PB90-100066/AS)

Coordination Activities

Intensive efforts are made to inform and involve the PHS and HCFA in the planning and implementation of the Agency's HIV research program. Activities include:

- Senior level participation in the biweekly meetings of the PHS Executive Task Force on AIDS and the PHS AIDS Leadership

Group, including membership of staff on five (5) of the working subgroups of the Task Force;

- Discussion of ongoing and proposed AHCPR activities with both PHS and HCFA representatives, including formal briefings at the PHS Executive Task Force on AIDS, the PHS Health Policy Data Committee, and an interagency meeting on primary data collection organized by the Office of Management and Budget;

- Participation in the annual interagency meeting on HIV research, sponsored by the Office of Technology Assessment, as a means to familiarize other agencies with AHCPR's program;

- Meeting with representatives of the National Institute of Allergy and Infectious Diseases (NIAID) to coordinate questions on the cost and financing of HIV services to be possibly included in the MultiCenter AIDS Cohort (MAC) Study and specifically detailed in the AHCPR's AIDS Cost and Service Utilization Survey (ACSUS); and,

- Review of the scope of work and products of AHCPR's ACSUS by various agencies, including efforts to assure that the survey design complements the ongoing work of HRSA, NIH, and AHCPR-sponsored grant research.

Department of Health and Human Services

Report on Activities in Aging

A Report to the
House Committee on Appropriations

January, 1990

DEPARTMENT OF HEALTH AND HUMAN SERVICES ACTIVITIES SERVING OLDER AMERICANS DURING 1989

In response to the many social, health, economic, and other needs of the Nation's elderly, a wide range of programs serving this age group were administered during FY 1989 by various agencies throughout the Department of Health and Human Services (DHHS). This report begins with a tabular summary of actual and expected annual expenditures for HHS activities on behalf of older Americans by each DHHS agency performing them. Narrative descriptions of those activities, as listed below, follow:

I. Office of the Secretary

   A. Federal Council on Aging

   B. Administration on Aging

II. Public Health Service

   A. Office of the Assistant Secretary for Health

   B. Health Resources and Services Administration

   C. Alcohol, Drug Abuse, and Mental Health Administration

   D. National Institute of Health

III. Health Care Financing Administration

IV. Social Security Administration

Office of the Secretary

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Funds for Programs on Aging
(in thousands of dollars) 1/

	1987 Actual	1988 Actual	1989 1/ Estimate	1990 2/ Estimate	1991 Estimate
I. Office of the Secretary (Older Americans Act)					
A. Title II, Federal Council on Aging	$ 200	$ 191	$ 188	$ 185	$ 185
B. Administration on Aging					
Title III-B, Social Services	$270,000	$269,029	$276,194	$272,961	$272,961
Title III Part C, Subpart 1 Congregate Nutrition Services	$348,000	$344,664	$356,869	$351,925	$351,925
Title III, Part C, Subpart 2, Home Delivered Nutrition Services	$ 75,400	$ 75,635	$ 78,419	$ 78,981	$ 78,981
Title III, Part D, Sec. 303, In-Home Services for Frail Older Persons	$ --	$ 4,787 3/	$ 4,826 3/	$5,756 3/	$ $5,756
Title IV, Training, Research and Discretionary Projects and Programs	$ 25,998	$ 23,935	$ 22,253	$ 25,332	$ 25,332
Title VI-A, Direct Indian Grants	$ 7,500	$ 7,181	$ 9,345	$ 11,108	$ 11,036
Title VI-B, Native Hawaiians			$ 1,365	$ 1,433	$ 1,505
White House Conference on Aging					$ 1,000

1/ All amounts in this tabulation are stated in thousands of dollars, except those relating to Social Security Administration and Health Care Financing Administration programs (which are stated in millions) and where otherwise marked.
2/ Title III and IV figures reflect reprogramming of $3,300,000 in 1989 to Title VI, with Congressional approved. All figures in this column are estimates, based upon 1990 Budget requests.
3/ 1988 is the first time funds were specifically appropriated for these services.

AGENCY FOR HEALTH CARE POLICY AND RESEARCH

AGING

OBLIGATIONS

FY 1987 Actual	FY 1988 Actual	FY 1989 Actual	FY 1990 Estimate	FY 1991 Estimate
$4,944,001	$5,898,826	$7,635,000	$9,780,000	$29,089,000

Alcohol, Drug Abuse and Mental Health

Aging Obligations

(Whole Dollars)

1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
$20,690,000	$23,014,000	$42,240,000	$47,135,000	$48,712,000

AGING

Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
Public Health Service:					
Health Resources & Services Administration:					
Bureau of Health Professions					
H.P. Special Educational Initiatives.....	$9,306,742	$12,439,317 1/	$10,653,123 2/	$9,823,000 3/	
Nursing Special Projects.....	983,887	2,019,980	2,412,811	2,654,092	--
Nurse Practitioners.....	1,237,145	1,366,940	1,460,069	1,560,000	--
Advanced Nurse Training.....	979,406	1,121,823	1,554,004	1,200,000	--
Area Health Education Centers.....	875,394	982,844	661,305	707,596	--
Physician Assistants.....	70,088	53,839	106,291	112,668	--
Family Medicine Residencies.....	2,996,066	1,998,669	1,481,819	1,511,455	--
Family Medicine Departments.....	419,642	--	403,025	411,086	--
General Internal Medicine & Pediatric Residencies.....	140,822	138,405	136,140	138,863	--
Podiatric Primary Care Residency Sec. 788(e).....	--	--	145,650	146,233	--
Geriatric Faculty Fellowships Sec. 788(b).....	--	--	3,100,000	3,121,700	--
Total.....	$17,009,192	$20,121,817	$22,114,237	$21,386,693	--

1/ FY 1988 Grants: S.788(d), 788(b) and 301/788 - $9,543,122; S.788(e) - $2,800,000.
Contracts: S.788(d), 788(b) and 301/788 - $96,195.
2/ FY 1989 Grants: S.788(b), 789(a) & 301 - $10,653,123.
3/ FY 1990 Grants: $9,823,000 (est.).

PROGRAM ON AGING
Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
Public Health Service:					
National Institutes of Health:					
National Institute on Aging	$177,461,000	$194,181,000	$222,545,000	$239,452,000	$248,938,000
National Cancer Institute	16,305,000	14,499,000	16,531,000	17,116,000	17,924,000
National Heart, Lung and Blood Institute	9,724,000	18,702,000	22,240,000	22,800,000	23,700,000
National Institute of Dental Research	3,165,000	3,746,000	5,483,000	5,691,000	5,876,000
National Institute of Diabetes and Digestive and Kidney Diseases	12,750,000	13,250,000	14,127,000	14,500,000	15,200,000
National Institute of Neurological Disorders and Stroke	26,523,000	30,867,000	33,141,000	34,198,000	35,773,000
National Institute of Allergy and Infectious Diseases	26,261,000	24,136,000	28,506,000	29,177,000	30,775,000
National Eye Institute	30,113,000	31,017,000	31,077,000	31,413,000	33,008,000
National Institute of Environmental Health Sciences	693,000	932,000	1,696,000	1,757,000	1,826,000
National Institute of Arthritis and Musculoskeletal and Skin Diseases	6,377,000	11,976,000	13,590,000	14,030,000	14,481,000
National Institute of Deafness and Communicative Disorders	1,278,000	1,222,000	1,511,000	1,898,000	1,983,000

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
Division of Research Resources.....1/	9,799,000	7,962,000	9,995,000	9,517,000	9,188,000
National Center for Nursing Research.....	2,889,000	2,872,000	3,295,000	3,750,000	3,750,000
Office of the Director.....2/	487,000	550,978	461,000	510,000	147,000
Total, NIH.....	$323,825,000	$355,912,978	$404,198,000	$425,809,000	$442,569,000

1/ This includes RCMI awards for FY 1989 - 1991. Prior to FY 1989, RCMI's were shown in OD.

2/ This includes AREA awards for FY 1987 - 1991, and RCMI awards for FY 1987 and FY 1988.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Funds for Programs to the Aged FY 1987 - FY 1991
(In Millions of Dollars)

	1987 Actual	1988 1/ Actual	1989 Actual	1990 Estimate	1991 Estimate
IV. Social Security Administration					
Benefit Payments to Persons Age 65 and Over from Social Security Trust Funds	$156,433	$165,993	$175,240	$187,432	$199,956
Payments to Persons Age 65 and Over From Federal General Revenue Funds:					
Supplemental Security Income Payments . .	4,182	4,433	4,360	4,176	4,705
Special Benefits for Disabled Coal Miners	853	826	808	793	769
Subtotal, Payments to Persons Age 65 and Over from General Revenue Funds	$5,035	$5,259	$5,168	$4,969	$5,474
Total, Social Security Administration . . .	$161,468	$171,252	$180,408	$192,401	$205,430

1/ Due to Federal legislation mandating check payment on a banking day, the SSI program made 13 monthly payments in FY 1988, will make 11 monthly payments in FY 1990, and 12 monthly payments in the other years.

Federal Council On The Aging

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Former Pima County Board of Supervisors and Business Owner
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Gloria Sherwood
Mental Health Practitioner and Real Estate Broker
Beverly Hills, CA

Albert Lee Smith, Jr.
Positive Maturity-Retired Senior Volunteer Program
Birmingham, AL

FACT SHEET

The Federal Council on the Aging (FCoA) was created in 1973 and is authorized under the Older Americans Act (OAA), as amended. The Council is composed of 15 members selected by the President and the Congress. Council members, who are appointed serve three-year terms, or continue to serve until they are reappointed or a successor is appointed. Members represent a broad cross-section of rural and urban older Americans, national organizations with an interest in aging, business, labor, and the general public. At least nine of the members must themselves be older individuals.

The President selects the Chairperson of the Council from among the appointed members. The Council meets, at the call of the Chairperson, at least quarterly.

Functions of the Council include:

- Reviewing and evaluating, on a continuing basis, those Federal policies, programs and activities, affecting the aging, which are conducted or supported by Federal departments and agencies in order to assess their value and impact on the lives of older Americans;

- Serving as a spokesperson for all older Americans by making recommendations to the President, the Secretary of Health and Human Services, the Commissioner on Aging, and the Congress regarding Federal policies which affect the aging and those federally conducted or supported programs and activities that impact on them;

- Informing the public about the problems and needs of the aging by collecting and disseminating information; conducting or commissioning studies and publishing their results; and issuing reports; and

- Providing public forums for discussing and publicizing the problems and needs of the aging, and obtaining information relating to those needs by holding public hearings and by conducting or sponsoring conferences, workshops, and other meetings;

- Preparing and providing for the President an Annual Report on the Council's activities and recommendations for the ensuing year.

Revised 5/4/88

ADMINISTRATION ON AGING

Title II of the Older Americans Act of 1965 (the Act) established the Administration on Aging as the principal Federal agency for carrying out the provisions of the Act. The 1987 Amendments to the Act reaffirmed the responsibilities of AoA, State Agencies, and Area Agencies to assure that community systems serving older people are established, strengthened, and extended throughout the nation. Through the Amendments, Congress also reaffirmed the need for strong partnerships and for effective coordination on behalf of older people. Congressional action also underscored concern for the most vulnerable elderly and emphasized the need to assure that priority focus is continued on the establishment and improvement of comprehensive coordinated community based systems of service.

The Older Americans Act seeks to remove barriers to economic and personal independence for older persons and to assure the availability of appropriate services for those older persons in the greatest social or economic need. The provisions of the Act are implemented primarily through a national "network on aging" consisting of the Administration on Aging at the Federal level, State and Area Agencies on Aging established under Title III of the Act, and the agencies and organizations providing direct services at the community level. In FY 1989, Congress appropriated $ 748,196,000 to support programs and activities to implement the provisions of the Act, which are administered by AoA. This excludes $ 188,000 available for the Federal Council on Aging under the Older Americans Act appropriation. (See Appendix I for a summary of AoA's budget for FY 1989.)

1. Role and Function of AoA

The Administration on Aging (AoA) is located in the Department of Health and Human Services (DHHS). The agency is headed by a Commissioner on Aging, who is appointed by the President with confirmation by the Senate and who reports directly to the Secretary. In April, 1989 Joyce Berry, Ph.D., was appointed Acting

Commissioner on Aging following the acceptance of the previous Commissioner's resignation. AoA programs are administered through a Central Office located in Washington, D.C. and ten Regional Offices. Title II of the Older Americans Act, as amended, describes the basic roles and functions of AoA. Chief among these are to serve as an effective and visible advocate for older persons (including American Indian, Alaskan Native and Native Hawaiian Aging) within the Department and with other agencies and organizations at the national level and to administer the programs authorized by Congress under Titles III, IV, and VI of the Act.

AoA provides policy advice to the Secretary of Health and Human Services in matters affecting older Americans and information to other Federal agencies and to Congress on the characteristics, circumstances and needs of older persons. The Agency also reviews and comments on departmental policies and regulations concerning services which affect the health and general well-being of older persons.

During FY 1989, the Administration on Aging continued its aggressive efforts to assist vulnerable older persons and their families in finding appropriate help to maintain their independence within their own communities and to delay or prevent unnecessary institutionalization. AoA believes that these efforts can best be achieved by providing State and Area Agencies on Aging with the flexibility that allows them to strengthen existing local systems to make them more visible, easily accessible, and responsive to the needs of older Americans, particularly the most vulnerable.

The building and strengthening of coordinated community services systems for older persons and their families continued to be the overarching goal of efforts undertaken by AoA during FY 1989. AoA continues to work with State and Area Agencies on Aging to develop ways in which all available resource groups (i.e., public, private and voluntary, as well as dedicated individuals) can effectively work together to create comprehensive and responsive community systems dedicated to maintaining the independence of older Americans.

Toward this end, efforts continue to focus on strengthening the roles of State and Area Agencies on Aging to help enhance, but not replace, individual self-sufficiency, family caregiving, and other traditional forms of community support. AoA recognizes that the Area Agency on Aging is the key organization that can forge the most effective and efficient linkages between existing systems of services within each community. Therefore, AoA works with State and Area Agencies on Aging to strengthen efforts that will build a system of services that provide a continuum of care for older persons, tailored to meet the needs and circumstances of individual communities.

2. Goals for Fiscal Year 1990 and Beyond

While working during Fiscal Year 1989 to accomplish the annual objectives related to the enhancement of community-based systems of services for older persons nationwide, the Administration on Aging began a developmental process for the establishment of goals for Fiscal Year 1990 and beyond. The process has been characterized by continuing dialogue with advocacy and interest groups in the field of aging including discussions with State Directors on Aging, with Area Agency Directors, service providers, the academic community, the Federal Council on Aging and with representatives of the Leadership Council of Aging Organizations.

As a result of the process the Administration on Aging (AoA) has selected eight areas of major activity in which goals have been established for Fiscal Year 1990 and beyond. These areas are: (1) Public/Private Partnerships, (2) Older Persons as a Resource, (3) Strengthening the Family and Generational Bonding, (4) Prevention and Alternatives to Institutional Care, (5) Promotion and Enhancement of Effective Community Based Service Systems, (6) Targetting - Strategic Resource Allocation, (7) Manpower Development and (8) Preparing for the 21st Century - Challenges and Opportunities of an Aging Society. (See Appendix VI for full Statement of Goals for 1990 and beyond.)

In the year 1990, the nation will celebrate the 25th Anniversary of the Older Americans Act of 1965. The Administration on Aging deems it important, as the

nation approaches the last decade of the 1990's and the Silver Anniversary of the Older Americans Act, to expand the agency's goal efforts and to assist the society in addressing policy issues which will undoubtedly carry over through the 1990's and beyond, into the 21st Century. It is important that our society becomes focused on the need to build adequate capacity to respond to the dramatic increases in the older population during the next century.

3. AoA - An Effective Advocate for Older Persons

As the focal point within the Federal government for aging-related concerns, the Administration on Aging provides leadership to other Federal agencies and to the several components of the national network on aging relative to their efforts on behalf of older persons. At the national level, AoA's leadership role places major emphasis on developing collaborative relationships with other Federal agencies to facilitate the development of methods to achieve a coordinated response to the needs, problems and concerns of older persons. Toward this end, AoA has developed and implemented a variety of special initiatives aimed at improving the quality of life for older persons. Examples of special initiatives undertaken during FY 1989 are described below under the Promotion and Enhancement of Effective Community-Based Service Systems Category and Health Category.

In addition to its Federal level advocacy responsibilities, AoA is also charged with assisting and supporting efforts by other components of the national aging network to serve as effective advocates at the State level and in communities across the country. Promotion of network visibility remains a key element in AoA's strategy for enhancing the network's advocacy capability. In its effort to make the public more aware of the network and what its components can do on behalf of the elderly, AoA has focused major attention on printing and distributing the generic booklet entitled "Where to Turn for Help for Older Persons". This booklet is aimed at linking middle-aged caregivers to resources and help for their older loved ones who live nearby or across the country. It answers some of the most frequently asked questions about finances, health,

legal and community services for the elderly. The Administration on Aging continues to receive a positive response about the booklet from public and private organizations, as well as the general public. Since it was first published in 1986, over 448,800 copies of the booklet have been reprinted by 80 organizations and companies including Levi Strauss, Blue Cross/Blue Shield, General Electric, United Auto Workers and the House Select Committee on Aging. During FY 1989, AoA continued efforts to secure support from private organizations for printing and distributing the booklet. In addition, AoA has also marketed the booklet through the Government Printing Office (GPO). Through the end of FY 1989, GPO had sold a total of 29,020 copies to the public.

o Community Achievement Award Initiative

The Administration on Aging implemented an initiative known as the Community Achievement Awards to recognize communities which have made significant progress in developing exemplary systems of services for older Americans. The awards are determined through a competitive process wherein each State is invited to nominate one of its communities for an award.

In July 1989, AoA honored ten communities with Community Achievement Awards in a highly publicized ceremony in Washington, DC. Awards were presented to communities in California, the District of Columbia, Illinois, Iowa, Montana, Nevada, New Mexico, North Carolina, South Dakota, and Wisconsin. Each State's Agency on Aging received a grant of up to $30,000 for post-award activities to encourage systems-enhancement in other communities throughout the State. These follow-up activities include developing resource brochures, producing video tapes or slides to publicize the award-winning system, and establishing Peer Counseling Teams to provide information and technical assistance to communities interested in enhancing their own systems of services for the elderly.

In addition, workshops, conferences, and training programs have been planned for a variety of organizations and individuals concerned with the elderly. The target groups include staff of Area

Agencies on Aging, local elected and appointed leaders, members of professional associations, persons working with senior citizens, and seniors themselves.

The FY 89 initiative has generated much publicity in the award-winning communities and States. Wide media coverage has been reported, including feature articles in newspapers and newsletters, and televised press conferences and interviews of community officials. In addition, the communities have been honored through proclamations from State Governors and have received recognition at meetings and annual conferences of organizations concerned with aging issues.

AoA has developed a brochure which describes each of the award-winning communities. Copies of the brochure have been sent to each State to use in these promotional activities.

The Community Achievement Awards initiative is in its second year.

o Low-Income Minority Elderly

The 1987 Amendments to the Older Americans Act require increased emphasis on meeting the needs of low-income minority elderly persons. The Administration on Aging has a major policy goal to enhance its commitment to develop and implement new strategies to more effectively target resources and programs on the needs of the most vulnerable older persons, with special emphasis on low-income minority elderly. We are confident that all segments of the national network of services for the elderly share our conviction that substantial improvement on this mandate can and must be achieved as a priority.

The Older Americans Act Amendments establish specific requirements for Area Agencies with respect to low-income minority individuals. Section 306(a)(5)(A) of the Act requires Area Plans to:

1. Provide assurances that preference will be given to providing services to older individuals with the greatest economic or social needs, with particular attention to low-income minority individuals;

2. Provide assurances that the Area Agency will include in agreements made with service providers a requirement that the provider will: a)specify how he intends to satisfy the service needs of low-income minority elders in the area served by the provider, and b) attempt to provide services to low-income minorities in at least the same proportion as the population of low-income older persons bears to the population of older individuals in the service area;

3. Identify the number of low-income minority older individuals in the planning and service area; and

4. Describe the methods used to satisfy the service needs of such minority elders.

States report a total of over 2 million low-income minority elders. Nearly one-third of these older persons are concentrated in the southeastern states of Georgia, Florida, North Carolina, and Alabama. Nation-wide, the largest numbers of low-income minority elders live in New York, Georgia, Texas, Florida, and California. The smallest populations of low-income minority older persons reside in New Hampshire, North Dakota, Idaho, and Nevada.

A wide variety of methods is used by States to satisfy the service needs of their low-income minority individuals. A high proportion of the States is actively involved in training and information dissemination, sometimes in languages other than English. Many States report increasing outreach and advocacy activities, working with national minority organizations, holding conferences, forming task forces, or altering their funding formulas to reach more low-income minority elders. Several States report targeting nutrition and senior sites and detailing minority action steps in their State Plans as important in their attempts to satisfy the service needs of this low-income minority elderly population. The Administration on Aging highlighted applications of these strategies and methods in a memorandum to States in Fiscal Year 1989.

o Community and Migrant Health Centers

The Administration on Aging, in collaboration with the Health Resources and Services Administration (HRSA), completed a two phase initiative designed 1)

to promote older persons having greater access to and participation in the primary care services of the Community and Migrant Health Centers (CMHC's) and, 2) to increase targetting of supportive services by AAA's. The approach was to forge stronger linkages between the two programs at all administrative and programmatic levels to ensure coordinated planning, integration of resources wherever possible, and the development of mutually supportive strategies at the State and local levels.

The Administration on Aging coordinated with the Health Resources and Services Administration in developing an evaluation of the linkages between the Community and Migrant Health Centers and the network of aging services. The goal of the evaluation, funded by HRSA, is to assess the initiative's impact, document exemplary practices of the community and migrant health centers for purposes of replication and document existing barriers preventing collaboration between the two programs. This project has been extended to enable the researchers to develop a set of policy and program recommendations for future directions.

Caregiving

Over the past few years, the public and private sectors have become increasingly aware of, and involved in, issues of caregiving that arise as a result of families, friends and neighbors supporting and providing assistance to an elderly individual. AoA has been working with both the public and private sectors to promote knowledge of caregiving and its corollary in the workplace, Eldercare.

AoA has collaborated with the Office of Personnel Management and the Department of Labor, among other Federal agencies to expand the existing knowledge base regarding Eldercare issues and caregiving in general. Extensive work is also being initiated with private sector organizations at both central and regional office levels. The private sector is recognizing Eldercare as a benefits issue and is initiating collaboration with local agencies operating under the auspices of the Older Americans Act.

The Administration on Aging Regional Offices have been successful in promoting strong public-private sector initiatives. They continue their efforts in:

1. promoting and supporting State efforts to implement caregiving initiatives in the public and private sectors;

2. developing options for public/private collaboration; and

3. helping to create options for business to initiate, such as accumulation of credit hours for caregiving, and banking pre-tax deductions for costs of adult day care and medical costs.

Older Volunteer Recognition Ceremony

In celebration of Older Americans Month, AoA hosted with the American Association of Retired Persons and the May Department Stores Company, a ceremony and reception to honor older volunteers. The event, held on May 24, 1989, in the auditorium of the Wilbur J. Cohen Building, recognized one individual from each State whose dedication and service was representative of all of the older volunteers in the State. HHS Secretary Louis W. Sullivan presented a plaque to each State designee.
Invited guests included representatives of Congressional committees and national organizations who work on issues affecting older people. There was extensive media coverage of the event.

Commissioner on Aging Roundtables

[illegible]ny issues impact on the Older Americans Act pr[illegible]rams. One mechanism utilized for discussion of these important issues was the convening of Roundtables with noted experts, representatives from national organizations, State and Area Agencies on Aging and service providers. These Roundtables provided an opportunity for dialogue, policy discussion and a mechanism for providing input into AoA policy deliberations.

The first Roundtable dealt with the issue of minority participation in Older Americans Act programs. The 1987 Amendments placed increased emphasis on serving

those in greatest economic or social need, with particular attention to low-income minorities. Among the issues discussed were: 1) intrastate funding formulas; 2) hiring minority staff; 3) site selection; 4) training aging network staff; and 5) minority contracting. Invited, were four minority aging organizations: the National Caucus and Center on Black Aged, the Asociacion Nacional Pro Personas Mayores, the National Asian/Pacific Resource Center on Aging and the National Indian Council on Aging. Directors of State Units on Aging, an Area Agency on Aging, an aging service provider, representatives of the National Association of State Units on Aging and the National Association of Area Agencies on Aging and the National Minority Aging Resource Center were invited.

A second Roundtable dealt with the important issue of eldercare. Business and corporate communities have demonstrated a growing commitment to assist employees who serve as caregivers for older relatives. In a number of instances, private sector groups have asked State and Area Agencies on Aging to provide assistance. The issues addressed at this roundtable focussed on ways in which State and Area Agencies on Aging can work with the business and corporate communities. The issues discussed ranged from statutory prohibitions to the public purpose mission of area agencies. Invited were the Illinois and Ohio State Directors on Aging, two Area Agencies on Aging Directors from Texas and Oregon and the executive directors of the National Association of Area Agencies on Aging and the National Association of State Units on Aging.

Housing

Under the Older Americans Act, the Administration on Aging (AoA) collaborates with the Federal housing programs in the Department of Housing and Urban Development (HUD) and the Farmers Home Administration (FmHA) within the Department of Agriculture. AoA activities include exploration of possible interagency agreements, mutual participation in conferences and provision of materials, and data exchanges between the respective networks. During the past year, AoA provided assistance to HUD in identifying and recruiting housing counselors for

training in the Home Equity Conversion (HEC) Demonstration Program. This HEC Demonstration Program will be explained further under the Title IV-B Research and Demonstration Projects of the Annual Report. The counterpart State and local agencies are encouraged to work together to provide opportunities for older citizens to have suitable housing alternatives which are affordable and which emphasize the need for maintaining a continuum of care for the elderly. AoA's regional office provided testimony before the U.S. Senate Budget Committee Hearing on congregate and supportive services in housing for the elderly in Atlanta, representing the Department of Health and Human Services at this Hearing. The Regional Office in Atlanta is currently planning a conference for February 1990 which will focus on "Aging in Place: Relating and Linking Congregate and Supportive Services in and to Housing for the Elderly".

Transportation

On October 24, 1986, the Secretaries of DHHS and DOT signed an agreement to facilitate effective and efficient coordination of specialized and human services transportation. Under this agreement, AoA co-sponsored the development of a guidebook on "Best Practices in Specialized and Human Services Transportation Coordination". In December 1988, AoA and the Urban Mass Transportation Administration (UMTA) entered into an Interagency Agreement to support the collaborative efforts between DHHS and DOT. Under this agreement, AoA and UMTA provided funds to the States of Texas and Ohio for convening workshops designed to further the goal of improving the coordination of transportation service systems. The first workshop was held on July 26, 1989, in Austin, Texas, the second one was held on September 22, 1989, in Columbus, Ohio. Both workshops brought together representatives of both the aging and transportation networks to discuss methods of improving the coordination of transportation systems in the two States. The guidebook on "Best Practices in Specialized and Human Services Transportation Coordination" was used at the workshops. The products of the workshops are State "Action Plans" detailing the responsibilities and steps to be taken by the aging and transportation networks to improve the coordination of

transportation service systems. These plans will be made available to all other States for replication in keeping with each individual State's priorities.

Employment

AoA conducted a discussion based on the Bureau of Labor Statistics report, Labor Market Problems of Older Workers. The report examines the extent of labor market problems of older men and women and documents the employment outcomes of those older persons who look for work following job loss or reentry into the labor market. Institutional impediments to employment, such as Social Security regulations, pension rules and policies, the market for part-time jobs and age discrimination, are also addressed. Representatives of the Leadership Council on Aging, DHHS, HDS Program Offices, and the general public were in attendance.

Supplemental Security Income (SSI), Food Stamp and Medicaid Outreach

The 1987 Amendments to the Older Americans Act require the Commissioner on Aging to analyze, compile, and distribute information about outreach activities targetted to older persons who may be eligible for, but are not receiving, SSI, Food Stamp, and Medicaid Benefits. The 1987 Reauthorization of the Older Americans Act provided for an authorization of $10 million for AoA to conduct outreach activities. Even though these funds were not appropriated, through the efforts of the AoA Regional Offices and the network on aging, AoA has been able to facilitate outreach activities at the State and local levels.

During FY 1988, AoA began distributing outreach materials to the States on the Supplemental Security Income (SSI), Food Stamp, and Medicaid Programs. Continuing this effort into FY 1989, arrangements were made for the Social Security Administration (SSA) to send SSI outreach materials directly to the States. AoA disseminated the brochure, "Facts About the Food Stamp Program" published by the Department of Agriculture's Food and Nutrition Service, and the SSA Fact Sheet describing two provisions of the SSI Program that were effective on July 1, 1988. Sharing

of information and materials between the Health Care Financing Administration (HCFA), SSA, and AoA at the Regional, State, and local levels is ongoing.

These efforts respond to the concern of Congress and the President that all older people be made fully aware of the benefits available to them under the SSI, Food Stamp, and Medicaid Programs and that eligible individuals be encouraged to apply. State Agencies on Aging were urged to review the available materials and to develop or strengthen effective outreach programs throughout the State to increase the participation of the elderly in the programs. AoA Regional Program Directors were asked to contact State Directors on Aging to offer their assistance in organizing Statewide outreach campaigns. AoA Regional Work Plan Accomplishments Reports indicate that most of the States have, or will develop, new SSI outreach activities.

Collaboration, Linkages, and Systems Building: AoA, SSA, HCFA Memorandum of Understanding

During FY 1989, AoA, SSA, and HCFA engaged in discussions on how the three agencies can work collaboratively to develop and coordinate programs that are accessible to all older people and that assure special help for the most vulnerable. These discussions resulted in a draft Memorandum of Understanding between the three agencies. Under this proposed agreement, AoA, SSA, and HCFA would jointly engage in collaborative activities to achieve the goal of promoting the well-being of older persons by providing a coordinated response to the needs, problems, and concerns of older persons. Such activities would support the following objectives - (1) to improve the coordination of services funded under the program authorities of AoA, SSA, and HCFA which relate to older persons; (2) to increase public awareness of SSA and HCFA entitlement programs, the nutrition and supportive services of AoA and other programs which promote the well-being of older persons; (3) to conduct outreach efforts designed to increase participation in SSA and HCFA entitlement programs, the nutrition and supportive services programs of AoA and other programs which promote the well-being of older persons; (4) to reduce dependency on entitlement programs; and (5) to improve health care for vulnerable older people.

Developmental Disabilities

Throughout FY 1989, AoA forwarded Information Memoranda to States which discussed the Older Americans Act Amendments of 1987 as they relate to older persons with developmental disabilities and shared selected examples of effective collaboration between the networks of AoA and the Administration on Developmental Disabilities. The AoA Regional Offices were provided information and resource materials to assist them in forging linkages and developing collaborative relationships with the ADD network.

Memorandum of Understanding between AoA and ADD--Areas of Federal, State, and local level collaboration between the AoA and ADD networks were identified at the February 1989 meeting of the University Affiliated Programs and at a subsequent meeting with the New York State Office of Mental Retardation. These recommended areas served as the basis for the June 27, 1989, Memorandum of Understanding between AoA and ADD. The purpose of the MOU is to improve the coordination of programs administered by AoA and ADD which relate to the welfare of older persons with developmental disabilities. Under this agreement, AoA and ADD will jointly develop and implement initiatives to (1) promote a better understanding between programs serving the elderly and persons who are disabled within the AoA and ADD networks, (2) improve the coordination of programs and services for older persons with developmental disabilities, and (3) promote the integration of these individuals into the mainstream of society. AoA and ADD will also undertake the development of other joint initiatives which promote the independence and well-being of older persons with developmental disabilities.

International Conference on Aging and Developmental Disabilities--AoA and ADD provided funding for the 1990 international conference on research and practices in the area of aging and developmental disabilities. The purpose of the international conference is to assemble a group of international researchers, practitioners, and public officials to discuss state-of-the-art practices in aging and developmental disabilities. The objective of the conference is to synthesize the current practice

and identify future areas of inquiry and program development. Conference participants will include individuals from Europe, Australia, and Hong Kong who are considered leaders in research or practice regarding older persons who are developmentally disabled. These individuals will interact with a selected group of national and State leaders within the United States and Canada with regard to research, practice, and public policy.

Interagency Agreement between AoA and the National Institute for Standards and Technology--Fire Safety in Board and Care Homes--The major development in fire safety in recent years has been the adoption of the Fire Safety Evaluation System for Board and Care Homes into the Life Safety Code (Chapter 21). This system was developed by the National Bureau of Standards (now called the National Institute for Standards and Technology (NIST). In April 1989, AoA entered into an Interagency agreement with NIST. The objective of the agreement is to assure a high level of fire safety in board and care homes and to decrease the cost of achieving such safety. Under this agreement, AoA is participating jointly with the Department of Education, ADD, and the Health Care Financing Administration in the funding of a project to evaluate the fire safety evaluation system in board and care homes and to foster the use of Chapter 21 with an emphasis on determining the scope of its current use and the degree to which its use is achieving the desired goals. The project will provide information regarding whether or not the use of the Chapter 21 model requirements provides a high level of safety at reasonable cost.

4. Title III Supportive and Nutrition Services

The Administration on Aging (AoA) is the lead component within the Department of Health and Human Services on all issues concerning Aging. It advocates for the needs of the elderly in program planning and policy development; provides technical assistance; issues best practices guidelines; and initiates policy relative to funding the States and Territories for the provision of services to older Americans according to Title III (Grants for State and Community Programs on Aging.)

Each State Agency is required to subdivide the State into Planning and Service Areas (PSAs) and to designate within each PSA an Area Agency on Aging (AAA) to be specifically responsible for carrying out the purposes of the Act within the PSA. While most States have a statewide network of Area Agencies on Aging, fifteen States/Territories have designated their entire geographic area as a single PSA with the State agency performing the Area Agency functions because of their small geographic areas or population size.

5. State Agencies on Aging

The Older Americans Act provides that the State Agency on Aging shall be the leader relative to all aging issues on behalf of all older persons in the State. This means that the State Agency proactively carries out a wide range of functions related to advocacy, planning, coordination, interagency linkages, information sharing, brokering, monitoring and evaluation designed to develop or enhance services for older persons throughout the State. Fifty-nine (59) States and other jurisdictions receive support under Title III of the Act. States may elect durations of two, three or four years for State and Area Plans.

The State Agencies assure that the resources made available to Area Agencies on Aging under the Older Americans Act are used to carry out the Area Agency mission of assisting older persons in leading independent, meaningful and dignified lives in their own homes and communities as long as possible.

State and Area Agencies on Aging work to facilitate the most effective use of all community resources, both public and private, to provide for appropriate services to older persons within the many communities of the Planning and Service Area. To effectively accomplish this goal, there must be a community-wide effort with all appropriate resources, programs and personnel carefully coordinated.

6. Area Agencies on Aging

In FY 1989, there were over 670 Area Agencies on Aging operating under Title III of the Act. As of the end of FY 1989, there were approximately 684

Planning and Service Areas, including the 15 Single Planning and Service Areas, previously mentioned, covering whole States and Territories. An Area Agency on Aging may be a public or private organization, an Indian Tribe or a sub-State regional body. Area Agencies on Aging have the major responsibility for the administration, at the sub-state level, of Title III funds for supportive and nutrition services. Area Agencies receive their funds from the State Agency on Aging and then award grants and contracts to local supportive and nutrition service providers under an approved area plan.

Area Agencies on Aging are responsible for providing technical assistance to and monitoring the effectiveness and efficiency of, their respective service providers. Through their coordination and planning activities, Area Agencies also address the concerns of older persons at the community level. Area Agencies interact with other local public and private agencies and organizations in order to coordinate their respective activities and elicit or "leverage" additional resources to be used on behalf of older persons.

Funding State and Area Agencies on Aging

State Agencies on Aging received a total of $715.2 million of Title III funds during FY 1989. Funds under this Title of the Act are made available to the States on a formula basis upon approval of State Plans by AoA Regional Offices. States then allocate funds to Area Agencies based upon approved Area Plans to pay up to 85 percent of the costs of supportive services and senior centers, and nutrition services. In most cases, Area Agencies on Aging then arrange with both nonprofit and proprietary service providers to deliver nutrition and other services described in the Area Plan.

In general, funds provided to Area Agencies are used for the administration and provision of a wide range of supportive and nutrition services authorized under parts B, C and D of Title III as described in the next paragraph.

7. Title III Services

Title III activities conducted in the States during FY 1989 were based upon State plans ranging in duration from two to four years. In FY 1989 four separate allocations under Title III were made to States for: (a) supportive services and senior center operations; (b) congregate nutrition services; (c) home-delivered meals; and (d) in-home services for the frail elderly. The 1987 amendments to the Older Americans Act newly established Part D to Title III for in-home services for the frail elderly. (See Appendix II for State allotments under Title III in FY 1989).

Title III-B supportive services are designed to provide assistance to all older persons, with particular attention to older persons in greatest economic or social need. Most supportive services fall in three broad categories: access services; in-home services; and other community and neighborhood services. Access services are transportation; outreach; and information and referral. Most in-home services are either homemaker; personal care; chore; and/or visiting and telephone reassurance. Community and neighborhood services include legal services; residential repair; escort services; health services; physical fitness programs; pre-retirement and second career counseling; and other services.

Data on Title III services and program operations are reflected in Program Performance Reports which are sent to AoA each year by the State Agencies on Aging through AoA's ten Regional Offices. The Title III Program Performance Reports for FY 1988 were analyzed during FY 1989. The national program statistics for FY 1988 are provided in Appendix III. These data pertain to: participation levels for Title III-B supportive services; service characteristics and participation under Title III-C nutrition programs; and Title III-D in-home services for frail older persons. Selected program data are presented in the following paragraphs.

The 1987 Amendments to the Older Americans Act require the Administration on Aging to report to Congress specific information regarding the programs and activities under the Act. Although this information was collected by the States for FY 1989, it will not be available until FY 1990.

8. Title III-B Supportive Services

In FY 1988, the Title III-B program reached an estimated 8.2 million older clients in need of access, in-home, and community-based services. In FY 1988, 16 percent of all participants were racial and ethnic minorities and 41 percent were low income. In the area of access services, transportation was the most frequently provided service, followed by information and referral, then outreach. Of four defined in-home categories, reassurance to elderly persons through visiting and telephone contacts was reported most frequently, followed by homemaker, chore, and home health aide services. Of the four services in the community and neighborhood category, health services were most frequently provided, followed by legal, escort, and residential repair/renovation services.

9. Title III-C, Congregate and Home Delivered Nutrition Services Congregate and Home-Delivered Nutrition Services, authorized by Title III-C, continue to be an integral part of the systems which communities are developing to assist their older citizens in maintaining independence and remaining in their own homes as long as possible.

Congregate Nutrition Services

Over 147 million congregate meals were served to older people and their spouses during FY 1988; this total represents an increase from the FY 1987 figure of 146 million. In addition to Title III-C funds, these meals are also supplemented and supported by United States Department of Agriculture funds; Social Services Block Grant program funds; and other Federal, State/local funds; and participant contributions. Over 2.7 million elderly received meals at congregate sites.

Home-delivered Meals

Home-delivered meals are also critical to the maintenance of independence for older persons who are unable to participate in congregate meals programs. During FY 1988, 94.6 million meals were provided to the homebound elderly from Title III-C and other funding sources. This number represents an increase over the 85.9 million home-delivered meals served in FY 1987. A total of 745,097 older persons received home-delivered meals.

10. Title III-D, In-Home Services for Frail Elderly

Title III-D, In-Home Services for Frail Older Persons was established by the 1987 Amendments to the Older Americans Act, and funds became available for the first

time in FY 1988. Title III-D program performance data for FY 1988 were optional and less than half of the State Agencies on Aging reported data. In FY 1989, State Agencies were required to submit Title III-D data, however, this information will not be analyzed until FY 1990.

Allotment Transfers

Under the Older Americans Act, the State Agencies on Aging have the authority to transfer limited amounts of funds among three of the Title III allotments (parts B and C) in order to better reflect their local needs and priorities. (See Appendix III for Title III State Allotments after Transfers in FY 2989.) In FY 1989 the net transfers were as follows:

	Net Transfers	Percent Change
Title III-B (Supportive Services)	+$26,349,922	+9.5%
Title III-C-1 (Congregate Nutrition Services)	-$58,550,969	-16.5%
Title III-C-2 (Home-Delivered Meals)	+$32,201,047	+41.0%

*Transfer as percent of original allotment.

Advocacy and Partnerships

In advocating for older persons, State and Area Agencies on Aging review and comment on State and community policies, programs and issues; provide testimony at public hearings; publish reports; coordinate and provide technical assistance to other public and private agencies and organizations; and leverage resources from other Federal, State and local programs, as well as private charitable and business resources.

Non-federal Resources and Program Income

The Title III program has evolved from a relatively simple program of community service projects for older persons into a complex and highly differentiated "national network on aging" currently consisting of 59 State Agencies and over 670 Area Agencies on Aging and more than 25,000 local nutrition and supportive service providers. These nutrition and supportive service providers are local public, private, or voluntary organizations. Not only do the State and Area Agencies on Aging use Title III monies to provide for services, they also are instrumental in leveraging other public and private monies in addressing the needs of older persons.

Title III regulations (45 C.F.R. Part 1321) require each service provider to "provide each older person [receiving services] with a full and free opportunity to contribute toward the cost of the service." Although AoA emphasizes through the aging network that this is not a fee and that contributions are entirely voluntary, these contributions have been steadily increasing, as follows:

FY 1981	$ 79.0 million
FY 1982	100.8 million
FY 1983	116.7 million
FY 1984	131.7 million
FY 1985	140.1 million
FY 1986	153.9 million
FY 1987	163.6 million
FY 1988	168.1 million
FY 1989	(Data unavailable until late December)

Ombudsman Programs

The State Agencies are authorized by Section 308 of the Act to retain a specified portion of their Title III allocations to help defray their administrative costs. In addition, State Agencies use part of their Title III-B (Supportive Services and Senior Centers) funds and funds from other sources to establish and maintain long term care ombudsman programs at the State and sub-State levels. Through their ombudsman programs, States have addressed such issues as nursing home regulations, abuse of residents' personal funds, and restrictions on access to nursing homes. Complaint statistics and program data for the FY 1988 reporting period were analyzed during FY 1989. Some highlights of these data are as follows:

- During FY 1988, the most recent period for which data are available, there were 578 sub-state programs.

- Total funding for State and local ombudsman programs in FY 1988 increased from approximately $20.3 million to about $23.3 million. In addition to Title III-B funds, State and local governments used funds from other sources, including State, county, and local revenues, grants under Titles IV and V of the Older Americans Act, and other funding sources.

- Nationwide, more than 10,300 people worked in State and local ombudsman programs during FY 1988, including professional and volunteer staff.

- Services to American Indian, Alaskan, Native, and Native Hawaiians

Title VI Grants for Native Americans

Under Title VI of the Older Americans Act, the Administration on Aging annually awards grants to provide supportive and nutritional services for older Native Americans.

In the Older Americans Act Amendments of 1987 (P.L. 100-175, signed November 29, 1987) a change was made in Title VI to add older Native Hawaiians to the American Indians and Alaskan Natives who were already being served by Title VI. When Title VI had first been added to the Older Americans Act in 1978, it was named "Grants for Indian Tribes." The Amendments of 1987 renamed Title VI and divided it into two parts. The new name of the title is "Grants for Native Americans." The two parts are Part A, "Indian Program," which includes older Indians and Alaskan Natives, and a new Part B, "Native Hawaiian Program," for older Native Hawaiians. The law stated that Title VI Part B would take effect only if the total appropriation for Title VI exceeded the appropriation for Fiscal Year 1985 (which had been $7,500,000). Thus. at the beginning of Fiscal Year 1989, no funds were available for Native Hawaiians, since the original appropriation had been only $7,410,000. The $7,410,000 was distributed effective April 1, 1989 to 181 Indian tribal organizations, for an average grant of $40,439.

Later in the fiscal year, however, Congress reprogrammed funds among the titles of the Older Americans Act so that a total of $10,710,000 was available under Title VI; this included $9,345,000 for the American Indians and Alaskan Natives under Title VI Part A, and $1,365,000 for Native Hawaiians under Part B. Of the $9,345,000 available under Part A, $7,410,000 had already been distributed to 181 tribal organization grantees effective April 1, 1989. Thus, the amount available for late supplements for Title VI Part A grantees was $1,935,000. (See Appendix V for amounts of Fiscal Year 1989 grants, including the supplements.)

The amount of $1,365,000 available for organizations serving older Native Hawaiians was awarded in September, 1989 to Alu Like, Inc., a statewide nonprofit organization in Honolulu, Hawaii. Their application described services which would be provided to older Native Hawaiians in the five major islands of the State. The plans included congregate meals, transportation, health awareness and screening, education and recreation classes, and individualized services including escort, friendly visiting, and telephone reassurance. They plan to develop service centers for older Native Hawaiians on each island, located on or near the Hawaiian Home Lands, which are areas for Native Hawaiians.

12. Office for American Indian, Alaskan Native, and Native Hawaiian Programs (OAIANNHP)

On May 19, 1989 the Commissioner on Aging established the Office for American Indian, Alaskan Native, and Native Hawaiian Programs within AoA. This new Office was charged with the responsibility to serve as the focal point within AoA for the operation and assessment of programs authorized under Title VI of the Older Americans Act (OAA) and to provide program and policy direction to the ten Regional Offices of AoA in the execution of their Title VI responsibilities. Additional functions of the Office are to serve as the effective and visible advocate on behalf of older Native Americans, to coordinate activities with other Federal departments and agencies, to administer and evaluate grants provided under the OAA to Indian tribes and public and nonprofit private organizations serving Native Hawaiians, and to collect and disseminate information related to the problems of older Native Americans.

Interagency Task Force on Older Indians

The 1987 Amendments in Section 134(d) directed the Commissioner on Aging to establish a permanent Interagency Task Force on Older Indians, with representatives of departments and agencies of the Federal Government with an interest in older Indians. The responsibility of the Task Force, as stated in the 1987 Amendments, is to report to the Commissioner at 6-month intervals on their findings and recommendations with respect to facilitating the coordination of services and the improvement of services to older Indians. The Task Force is to be chaired by the Associate Commissioner on American Indian, Alaskan Native, and Native Hawaiian Aging who is to be appointed by the Commissioner. At the end of the fiscal year, plans were underway for convening the Task Force.

AoA Discretionary Programs

Title IV-A- Education and Development Projects

Sections 410 and 411 of the Older Americans Act authorize the award of grants and contracts to assist in recruiting persons, including minorities, to enter the field of aging; to train professional and paraprofessional persons employed in or preparing for employment in fields having an impact on the aging; and to provide technical assistance and other activities related to training. Other section of Title IV authorize health promotion projects and projects in long term care.

Several of the AoA National Goals for FY 1990 constitute an organizing framework for describing AoA's education development initiatives in FY 1989. These goals are:

- Manpower Development
- Targetting -- Strategic Resource Allocation
- Promotion and Enhancement of Community Based Service Systems
- Prevention and Alternatives to Institutional Care
- Public Private Partnerships
- Strengthening the Family and Generational Bonding

Highlighted below are new and continuing education and development project activities for FY 1989 under each of these six (6) AoA national objectives, grouped according to specific focus areas.

Manpower Development

The primary objective of the education and training program is to improve the quality of service and to help meet critical shortages of adequately trained personnel for programs in the field of aging. Specifically, activities supported under this program support the AoA Objective of promoting State and community leadership as they endeavor to meet the need for qualified individuals to assume leadership roles in developing and implementing responsive community-based systems of care for the elderly.

In FY 1989, AoA awarded eighteen (18) new grants in three training areas. A brief description of some of the major activities which these projects will undertake is presented below along with a description of major ongoing projects funded in FY 88:

A. National Leadership Institute on Aging During its first year the activities of the Institute focused on the development of program philosophy, conceptual framework, curriculum and other design and implementation tasks. These activities included the development of curriculum modules, program agenda and training materials, hiring of staff, selection of training site, faculty selections, establishment of an Advisory Committee which was convened twice, development of participant selection procedures, and design and dissemination of promotional materials.

Two five-day residential seminars were successfully conducted in May and September, 1989, for approximately 65 participants. The residential seminars, the core of the program, are intended to assist aging network executives to examine and develop their leadership styles and capacities and to challenge and inspire them to seek new ways to fulfill their roles as key policy makers in our rapidly expanding aging society. The response of the participants to the training program has been overwhelmingly positive.

B. Native American Leadership Institute In FY 1988 one (1) grant was awarded to Three Feathers Associates to conduct a training program for Title VI Directors. The first Native American Leadership Institute on Aging was held August 13-23 in Alexandria, Virginia and provided comprehensive training to Title VI Directors. The training increased the competencies and leadership skills of the Title VI Directors in administering and managing multi-service aging programs for Indians and Alaskan Natives. Segments of the curriculum included legislative and administrative history of aging services, program planning and implementation, program management and gerontology issues.

The Institute training encouraged networking between Title VI projects and enhanced the Title VI Director's understanding of community-based care systems development which will enable them to improve linkages with State Agencies on Aging and Area Agencies on Aging.

C. Career Training for Professionals and Paraprofessionals

A wide variety of professional and paraprofessional occupations significantly impact the lives of older people. To affect this population the Administration on Aging encouraged the inclusion of aging content in programs leading to certification or academic degree for persons in the field or preparing to enter these fields as an area of priority. Programs targeted to benefit from specialized gerontological or geriatric content in their career preparation include, physical therapists, counselors, occupational and recreational therapists, home economists, pharmacists, home health aids and others.

Ongoing Projects In September, 1988, nineteen grants were awarded in this category; four have reached their completion date and the other fifteen are due to come to a close in the first three months of 1990. Each program chose a unique and individualized method to achieve the, more or less, common objective, to include gerontological content in their curriculum in the present and as an existing part of future instruction.

Examples of the types of projects funded are: (1) initiate a "teaching nursing home" and develop an assessment tool to identify at-risk community elderly and (2) improve counseling services to older persons by increasing and institutionalizing gerontological counseling concepts and courses into existing counselor preparation programs.

As a part of the career preparation for professionals and paraprofessionals training priority area, Gallaudet University, Washington D.C., was awarded a two year grant to develop a curriculum in aging and hearing impairment to train graduate level social workers in the knowledge, values, and skills necessary to work effectively with hearing impaired older persons. The project is designed to produce a sequence of courses and field instruction for a specialization in gerontology and hearing impairment and to produce a cadre of social workers who can provide direct services, participate in community planning and conduct research for the benefit of elderly persons who are hearing impaired.

New Projects During FY 1989 AoA awarded seven (7) new grants to institutions of higher education for gerontological training and development projects. These projects have focused on several key areas including faculty development in gerontology, replication of successful curricula in institutions where gerontology has not been taught as extensively, and development of gerontological faculty and programs in minority institutions. Examples of projects include: (1) a project to provide gerontological training to faculty of 25 American Indian colleges; (2) replication of a successful gerontological social work curriculum in seven institutions in Hawaii and the Pacific Islands; and (3) development of gerontological programs in several New York City institutions with high minority enrollments.

D. Short Term Training and Continuing Education

Ongoing Projects Fourteen (14) FY 88 in-service training and continuing education grants were ongoing in 1989. These had been awarded to State Agencies on Aging, academic institutions, and national aging and

professional organizations to develop and conduct training activities for persons currently employed in occupations serving the elderly. Occupational groups represented in these projects include hospital discharge planners, social workers, home health and nurses aides, ministers, nursing home administrators, residential care managers, physicians, dentists and pharmacists.

New Projects In FY 1989, eight (8) grants were awarded to academic institutions, national professional organizations, and State Agencies on Aging to develop and conduct short-term training activities for persons working with or planning programs for the elderly. Occupational and professional groups targeted in these grants include in-home health and personal care workers, managers of elderly housing, hospital discharge planners, social service agency case managers, parole officers, and speech and hearing therapists, and academic teachers and researchers.

Seven projects will develop and pilot test training curricula and materials in topical areas of specific focus on special populations including, minorities, the frail and disabled, victims of dementia and elder abuse, older parolees, and low income housing tenants. The remaining project will place post-doctoral researchers and educators in aging and health care planning and service organizations to conduct three month planning, evaluation, and research studies guided by their host institution.

E. National Projects to Improve Accreditation Requirements in Aging--Ongoing Projects Four (4) projects awarded to national professional organizations in FY 1988 to develop programs on improving the instructional content in gerontology and aging-related knowledge and skills in the fields and professions of homemaker-home health aides, physical therapists, social workers, nurses and counselors made substantial progress towards completion of their objectives.

A common feature of these grants is the involvement of nationally known experts in these fields as members of working advisory boards, staff or consultants. They are helping to refine the competency standards of persons who work with the elderly in their field. Competencies are defined as the ability to demonstrate and apply

specific skills, knowledge, and attitudes which are used in working with older persons or in the conduct of work which has a substantial impact on the life of older persons. When consensus is reached, competencies are directly translated into professional and paraprofessional preparation, certification examination, and employment standards.

F. Minority Management Traineeship Program

Ongoing Projects

In FY 1988 The Administration on Aging awarded ten (10) grants in the area of Minority Training and Development. This priority area is designed to stimulate opportunities for training and the employment of minorities for management positions in the aging network. Five (5) of these grants were awarded to academic institutions, including two (2) Historically Black Colleges and Universities, two (2) to National Hispanic Aging Organizations, one (1) to a State Office on Aging, one (1) to a City Office on Aging and one (1) to a State Association of Councils on Aging. This represents a total of 101 trainees to be placed in State and Area Agencies on Aging and social agencies serving the elderly for administrative and managerial training. At the completion of the training period the trainee is expected to be hired in an administrative or managerial position by the host agency. If employment is not available in the host agency, the trainee will be assisted by the host agency and the grantee in locating employment in the aging network.

New Projects In FY 1989 AoA awarded three (3) new awards for Minority Management Traineeship projects. Each of the grantees are national minority aging organizations which will conduct nationwide traineehip programs in a variety of organizational settings leading to management and administrative positions.

2. Targetting -- Strategic Resource Allocation

HBCU Initiative -- Health Promotion Among Minorities

Ten (10) projects were awarded under the FY 1989 AoA Historically Black Colleges and Universities Initiative (HBCU). The initiative is designed to meet the health

promotion needs of older minority people. Louis W. Sullivan, M.D., U. S. Secretary of Health and Human Services, said that "too many Americans, especially among minority populations, are not getting help or information about preventing disease." Research has indicated that, often, minority elderly are disproportionately impacted by negative variables that influence their health and that they are more likely to be disabled and see themselves as being in poor health than elderly white people. Evidence indicates that there is an urgent need to provide information about, encourage and motivate older minority people to adopt good physical and mental health practices. In addressing the issue, AoA responded to Presidential Executive Order 12677 which asks Federal agencies to support HBCUs and to enlist their participation in agency efforts to meet their mandates.

3. Promotion and Enhancement of Community Based Service Systems

A. National Aging Resource Centers on Long Term Care Ongoing Projects

Six national Aging Resource Centers on Long Term Care were established in FY 88 for a three year period to provide training and technical information to State and Area Agencies on Aging in order to assist them in working with communities, public and private agencies, professionals and the public in implementing and coordinating programs and activities in a variety of topical areas. All six Centers were refunded during FY 1989.

Each Center has a specific expertise in a field of long term care. These include case management and assessment, quality assurance, data collection and analysis, long term care management of Alzheimer's Disease Patients, Medicaid coordination, supply and training of home care personnel, and supportive services and arrangements in adult housing. Centers collect information and research results, produce issue synthesis papers, and provide consultations, training and technical assistance to State and Area Agencies in their chosen areas of emphasis.

The Centers and the Administration on Aging work jointly to develop work plans under the Centers cooperative agreements. During their initial year, each Center

developed a national advisory committee which included representation of State and Area Agencies on Aging and experts in long term care. All Centers conducted a needs assessment of State and Area Agencies to establish and prioritize needs within Center topical areas. The results of this assessment were used to develop both the first year and future year work plans for each Center. Following are brief descriptions of Centers which include their description of their mission, core topics within this mission, and products which were worked on or completed in 1989.

The National Aging Resource Center on Long Term Care - Planning and Management of Community-Based Care at the Bigel Institute for Health Policy, Brandeis University, utilizes faculty and staff to assist State Agencies on Aging in strengthening their policy-making, program planning and program implementation capacities in the delivery of coordinated, community-based long term care services. During Year 1 the Center's topical modules were: (1) integration of health and long term care financing and service delivery systems, and (2) exploring best practices for recruitment and retention of in-home workers with effective monitoring. Issue papers on home care personnel, the Medicare catastrophic coverage act, long term care financing and delivery, and developing private markets in long term care were published. The Center conducts numerous major training and responds to individual requests for technical assistance.

The National Aging Resource Center on Long Term Care - Decisions by Older Persons, Families and Providers (DECISIONS) at the Schools of Public Health and Public Administration, University of Minnesota, utilizes faculty and staff to assist State and Area Agency administrators, planners, and policy makers in planning and implementing long term care service systems, including case management, which incorporate decision making by older persons, their families and professionals care givers. During its first year of operation, the Center synthesized existing functional assessment instruments covering physical, mental, cognitive, social interaction, and social supports which are in use or have been tested by health care and social service agencies and organization. The Center publishe

a newsletter, conducts periodic conferences in Minnesota and selective national professional association meetings, and responds to individual requests from State and Area Agencies on Aging for consultation.

The National Aging Resource Center on Long Term Care - Linkages between Aging Network, Hospitals, and Residential Facilities at the University of California at Los Angeles in collaboration with the University of Southern California, utilizes faculty and staff to promote better health-care partnerships among State and Area Agencies on Aging, hospitals and long term care facilities, decrease fragmentation and encourage more appropriate utilization by providers and consumers of the full range of options available to older persons to remain independent. The Center provides training and technical assistance to State Agencies in the areas of discharge planning, respite care, geriatric assessment programs, supportive housing and home modifications. Publications include a newsletter and materials on housing and home modification, respite care, emergency medical services and the Prospective Payment System.

The National Aging Resource Center on Long Term Care - State Management of Community-Based Care Systems at the National Association of State Units on Aging, provides assistance to State Agencies on Aging that are integrating major community care components into cohesive service delivery systems. Major emphasis is placed upon development of new approaches for quality assurance and strengthening linkages among acute, primary and institutional care systems. During its first year of operation, the Center conducted teleconferences on State legislation and case management, with published proceedings, produced a Medicaid Orientation Guide, reports on minority elderly needs and quality assurance issues, and is developing a Case Management Policy Manual and Compendium of Training Materials. The Center disseminates a newsletter and information packets addressing emerging long term care issues, conducts periodic training conferences at regional and national association meetings, and responds to State Agency requests for on-site and telephone technical assistance.

The National Aging Resource Center on Long Term Care - Alzheimers Disease and other Dementias at the Suncoast

Gerontology Center, University of South Florida is designed to respond to the needs and priorities identified by State Agencies on Aging as they plan, develop and implement programs and services for Alzheimer's Disease victims and their family caregivers. The Center provides State Agencies with information, national and regional training sessions, and technical assistance in establishing effective, comprehensive and coordinated statewide service systems and programs to recognize, diagnose, and provide short term treatment and long term management to Alzheimer's Disease patients, and meet the needs of their family caregivers. Center publications include a newsletter and applied research products, including best practice guides for educating minority caregivers, providing respite care, and evaluating day care centers.

The Heartland Center on Aging, Disability and Long Term Care at the National Center for Senior Living and the School of Public and Environmental Affairs, Indiana University at Indianapolis, utilizes faculty and staff resources from the multi-campus Indiana University systems, the University of Notre Dame and Purdue University Indian University, to provide technical assistance that meets the data needs and practices of State and Area Agencies on Aging in long term care planning and data analysis. The Center trains planners through workshops at national meetings, through site visits, and through a practitioner fellowship program. Information about selected data-based studies on special populations, such a minorities, low income, rural elders and disabled are disseminated through special reports and a national newsletter. Two special reports under development during the first year were a resource guide on use of national long term care data bases and a best practice guide on assessing needs of older persons.

Community Focal Points

Recognizing the important role which community focal points can play in community based systems, in FY 1989 AoA awarded two projects to encourage the development of senior centers as community focal points for older persons. One is a contract to provide technical assistance and training to the States and will focus on access and responsiveness of services. Training

attendees will include representatives from State Agencies on Aging and Area Agencies on Aging and AoA Regional Offices. Products will include a brochure and a technical handbook.

The second project is a two year grant to the develop a model rural focal point system in Nebraska. It will develop, evaluate, and disseminate a methodology for the development of community focal points in rural areas. It will also create a resource manual adapted to suit a rural environment and develop models for state and community resource councils. A video training package for workshops will also be produced.

C. Center for State Long Term Care Ombudsman Resources.

This Center is operated by the National Association of State Units on Aging in cooperation with the National Citizens Coalition for Nursing Home Reform. The Center's primary focus is on building Statewide systems of ombudsman services to address the issues facing older residents in long term care facilities. The Center initiated a number of activities during its first year including: development of a State Ombudsman Resource Manual; multi-regional teleconferences for information sharing with and among States; a National Training Conference for ombudsman and State staff; two training modules for States to use in training local ombudsman; a simplified guide to OBRA legislation; and a bi-monthly Center newsletter called the "Ombudsman Reporter". In addition to the Resource Center's responsibilities for technical assistance and training for states, the Center is conducting a study of ombudsman services to residents of board and care facilities. One section of this study is devoted to use of volunteers.

4. PREVENTION AND ALTERNATIVES TO INSTITUTIONAL CARE

During 1989 AoA carried out a wide range of activities addressing the theme of prevention of dependency. Many of these centered on health promotion and disease prevention--both through funded projects and through special initiatives and interagency activities. This section will describe the 1989 activities in this area.

A. Health Promotion -- Funded Projects

National Resource Center on Health Promotion and Aging

In FY 1988 AoA awarded a three year cooperative agreement to the American Association of Retired Persons (AARP) to establish a National Resource Center on Health Promotion and Aging. The principal mission of the Center is to serve the State Units on Aging by providing training and technical assistance as well as providing information and other resources to agencies and organizations who are interested in health promotion and older adults.

In 1989, the Resource Center conducted a comprehensive needs assessment of the 59 State Units on Aging to determine the extent of health promotion activities and needs throughout the country. In addition, the Center continued to expand its activities with presentations to Directors of State Units on Aging at three Regional Offices of AoA and visited several other States. The Center disseminated thousands of copies of brochures about the Center and a quarterly health promotion newsletter; is developing a video on health promotion for minorities; and is providing intensive technical assistance to State Units on Aging.

AoA refunded the Center in FY 1989 for a second year of operation during which the Center will continue and expand its training and technical assistance to the States and will also focus on minority issues and will develop an extensive resource library. The Center is assisting in collaboration with National Council on Patient Information and Education in disseminating resource materials on patient education in support of "Talk About Prescription Month" in October.

Prototype Health Promotion Projects -- SECTION 422(a)2

Ongoing Projects

Nine (9) projects were awarded under the Fiscal Year 1988 priority area "Education for Self Care." All were awarded to public and private institutions of higher education. The purpose of this priority area was to solicit proposals for the design and development of prototype health education and promotion programs that could be adopted by States and their Area Agencies on

Aging. Section 422(a)(2), authorizes AoA to support these activities at public or private institutions of higher education with graduate programs that have capability in the areas of public health; medical science; psychology; pharmacology; nursing; social work; health education; nutrition; or gerontology.

Prevention of Fire and Smoke Related Injuries and Death

Four (4) projects were funded in FY 1988 which focused on two aspects of improving in-home fire safety for older persons: (1) public education and (2) programs to assist older persons to make necessary modifications to their living environment to minimize the risk of fires. Products thusfar developed have proven to be excellent. These include a 30-minute video, Public Service Announcements, brochures, training manuals, a research paper, and items to be used at meal sites including placemats, bill stuffers and posters. Additional, many hours of successful training of older persons, firefighters, family members, caregivers and service providers have been accomplished.

Alcoholism As part of both the Secretary's Initiative on Indian Alcoholism and the Departmental Initiative on Alcoholism, AoA continued its health promotion efforts in this area. The three projects awarded to Indian Reservations in 1988 to assist in developing alcoholism prevention and education programs for older persons and their caregivers continued their activities and will conclude in 1990. Four additional projects were in funded in 1989, also in response to the recommendations on Alcohol Use and Abuse from the 1988 Surgeon General's Workshop on Health Promotion and Aging. Two (2) projects are studying study alcohol abuse and alcoholism among the aged. Two (2) additional projects are developing model educational programs for older persons, their families, and formal and informal caregivers to recognize and seek help for problems related to alcohol use and abuse.

American Association of Dental Schools (AADS)

In FY 1987, a grant was awarded to the American Association of Dental Schools (AADS) to expand and improve the predoctoral curriculum in geriatrics in U.S.

dental schools. The completed product, The Geriatric Dentistry Curriculum Resource Book, has proven to be an outstanding publication which is currently being widely disseminated.

Additionally, AADS was funded in FY 1988 to improve the geriatric education provided by the U.S. Dental Hygiene schools. AADS will establish guidelines in dental hygiene, produce a resource book similar to the one described above, and present resource material to faculty during a two-day workshop.

New Projects The FY 1989 AoA Discretionary Funds Program Announcement, in keeping with Section 422(a)(2) of the 1987 Amendments of the Older Americans Act, encouraged institutions of higher education to submit applications for prototype health education and promotion programs. Nine (9) new projects were funded and will focus on the following health promotion topics: nutrition education for Native Americans; injury prevention; smoking cessation; hearing impairment; physical fitness and exercise; and alcoholism. Most of theses projects include the development and testing of prototype or model health education and health promotion programs which can be [illegible]ted or replicated by a State or in other States. [illegible]scretionary grants funded this year, as well as those funded in the last two years, will continue to help support AoA's substantial health promotion efforts.

Another health related project was funded in FY 1989 as a field initiated demonstration project. This project will involve educating pharmacists throughout Florida about the cause, prevention and treatment of Diabetic Retinopathy, as well as how to provide effective patient and community education. In turn, the pharmacists will provide widespread education to various groups including Blacks, Hispanics, Native Americans, and those of low or fixed incomes.

B. Health Promotion -- Special Initiatives and Interagency Activities

National Health Promotion Initiative

The National Health Promotion Initiative for Older Persons is a joint activity sponsored by the Administration on Aging and the U.S. Public Health Service. This multiyear activity was officially

launched in 1984 with the signing of the first of several Memoranda of Understanding between the two agencies. The Initiative is designed to improve the health status of older persons and improve the quality of life of their later years.

The Initiative has three major goals: (1) maximizing the opportunities for older persons to live independently through improvement of their health status; (2) focusing attention on health promotion and disease prevention through improved nutrition; physical fitness; smoking cessation; mental health; dental health; adult immunization; prevention of fire and smoke related accidents and injuries; and driver and pedestrian safety; and (3) curtailing health expenditures caused by preventable conditions. Some specific activities conducted during FY 1989 to attain these goals are discussed below.

Administration on Aging/U.S. Public Health Service Memorandum of Understanding

In 1989, AoA and PHS renewed their joint agreement on the health promotion initiative, which has been in effect since 1984. The revised Memorandum of Understanding (MOU) is a collaborative effort with the various agencies which participate in the Health Promotion Initiative, including AoA and the following PHS agencies: the Office of the Surgeon General: the National Institute on Aging; the Office of Disease Prevention and Health Promotion; the Health Resources and Services Administration; the Food and Drug Administration; the Centers for Disease Control; and the National Institute of Mental Health. The Memorandum of Understanding will serve as the working agenda for the health promotion initiative for the next two years. Special emphasis will be on revitalizing Statewide health promotion coalitions. Priority areas for 1989 are: alcoholism, smoking cessation, nutrition, injury prevention, and exercise. For 1990, the priorities are: diabetes, depression and hearing impairments.

Smoking Cessation The Administration on Aging, in conjunction with the Office of Smoking and Health, the Office of Disease Prevention, and the American Association of Retired Persons, began the development of an initiative to encourage older persons that "It's

Never Too Late to Quit Smoking." The initiative, which is a follow-up to the recommendations of the 1988 Surgeon General's Workshop on Health Promotion and Aging, will include a public education and awareness campaign on the possibilities for stopping smoking at any age and will encourage older persons and their families and caregivers to seek the necessary resources to assist them in this effort.

Other Health Promotion Activities. The Administration on Aging supported the development and distribution of the fourth annual Health Promotion Calendar for Older Persons. Owing to the success of the prior calendars, the 1989 calendar was a joint effort between AoA, the National Council on the Aging and a private sector sponsor.

The Administration on Aging again collaborated with the National Osteoporosis Foundation to produce a poster and materials in support of National Osteoporosis Month. This activity is designed to raise national awareness of the prevalence of this disease among older persons and the possibilities which exist for prevention through modification of lifestyles.

C. Technology and Aging

Another area in which AoA promoted alternatives to institutional care is in through the use of technology to help meet the needs of older people. In 1985, AoA entered into an agreement with the National Aeronautics and Space Administration (NASA), the National Institute on Aging (NIA), the Veterans Administration (VA), and the National Institute on Disability and Rehabilitation Research (NIDRR). The purpose of this agreement is to collaborate on using NASA aerospace technology and scientific knowledge about aging to develop, produce and market devices to assist the elderly. As a result of this agreement, a prototype device to notify caregivers of wandering behavior by impaired older persons is being developed through a contract with Cortrex Electronics, Inc. The next step in this project will be clinical trials of the device.

In addition, the agencies convened a roundtable of experts in December, 1988, on the seating and mobility needs of the elderly. A report was developed on the findings of the roundtable regarding the status of current technology and specific needs for further research and development.

Small Business Innovation Research Program

During FY 1989, five Phase II contracts were awarded under the Small Business Innovations Research Program (SBIR) to projects originally funded in FY 1988. These contracts address the issue of the application of technology to help meet the needs of older persons. Under the Small Business Innovation Development Act (P.L. 97-219) DHHS and other federal agencies set aside a specified portion of their research and development funds for an SBIR Program. The legislation is designed to stimulate technological innovation; use small business to meet federal research and development needs; increase private sector commercialization of innovations derived from federal research and development; and foster and encourage participation by minority and disadvantaged persons in technological innovation.

SBIR is a three phase program. The Phase I contracts awarded in FY 1988 concluded in November 1988. In FY 1989, five Phase I contractors competed successfully for Phase II awards. Three contracts are for development of simple, low cost products that could enable older people to perform the tasks of daily living. Two contracts are for the development and implementation of a service delivery model that combines the use of low technology devices and traditional supportive services to effect greater independence by frail but mentally alert older persons.

5. PUBLIC PRIVATE PARTNERSHIPS

A. Corporate Eldercare

Increasing numbers of individuals have dual responsibilities as employees and as caregivers for older relatives. This has brought the issue of caregiving into the workplace. Corporations are beginning to recognize that the stress resulting from the uncertainties and responsibilities of caring for an older relative takes its toll in the workplace through lower morale, absenteeism and decreased productivity.

This project provided intensive training in caregiving and aging issues to corporate human resource and employee assistance professionals in 12 cities across the country through teleconferencing technology. The AoA funded teleconference was developed and produced by

the University of Bridgeport and the National Council on the Aging. It was supported in part by the American Association of Retired Persons and hosted by a corporate sponsor at each site. The project also focused on developing linkages between the employee assistance professionals and the State Agency on Aging through direct participation of State Directors on Aging at teleconference sites and through aging network involvement in the development of resource materials.

B. Other Partnerships with Business

Washington Business Group on Health (WBGH). WBGH is a national membership organization representing over 200 local business/health coalitions. This project has focused on the development of 12 model partnerships between business/health coalitions and the aging network. Four of these have been devoted exclusively to issues facing employed caregivers of older relatives. The remaining eight "mini-grants" are devoted to aging program development in a variety of areas including work and retirement, health promotion and health education.

The project is producing an excellent bi-monthly newsletter entitled "Together in Aging". Also, the project is nearing completion of a background paper and policy report for employers on the issue of caregiving as well as training materials for Area Agencies on Aging on encouraging corporate involvement in caregiving programs.

In addition, project activities have been highlighted in a number of public forums. Some of these include a Congressional forum on public/private partnerships in eldercare co-sponsored with Olympia Snowe and John Glenn (November, 1988) and conferences co-sponsored with the National Association of Manufacturers (January, 1988) and the American Society on Aging (March, 1989).

C. National Energy and Aging Consortium. The Consortium is a coalition of national public and private sector organizations concerned about the energy related needs of the elderly. Energy related needs involve a broad spectrum of issues such as housing, assistive devices in the home, low income energy assistance and others. AoA

takes an active role in the Consortium and serves as a member of the Steering Committee. A major focus of the Consortium is the development of State energy and aging consortia. To date, 14 such consortia have been established. During 1989 the Consortium's primary activity was to plan and convene a major national conference entitled "Building Better Partnerships: Energy and the Elderly in the 1990's" in Tulsa, Oklahoma in collaboration with the Oklahoma Energy and Aging Consortium.

6. Strengthening the Family and Generational Bonding

Intergenerational programming has emerged as a creative way of maximizing resources and meeting the needs of young and old. It is the caregiving system which helps the elderly person remain in the community setting, and it is the breakdown of this system which contributes to institutional placement. In an effort to provide respite care to families caring for physically and mentally disabled elders, project "Time Out' - an intergenerational approach to respite care - was conducted by Temple University. This project demonstrated that an intergenerational approach to providing respite services is viable. Families who received services found the program very helpful. When supported by appropriate services, the families can nurture and care for their elders within the community. Information and materials for replication developed by this project include: (a) a 7-12 minute slide/tape show, (b) The Respite Worker's Handbook, (c) The Trainer's Manual, (d) Time Out brochures and posters and (e) A Program Development Manual.

Title IV-B: Research and Demonstration Projects

Title IV-B of the Older Americans Act authorizes funding for research and demonstration projects to identify, assess and demonstrate new approaches and methods to improve the well-being and independence of older persons. The primary objective of AoA-supported research and demonstration projects is to assist in establishing, in every community of the nation, a comprehensive system of community services that responds to the talents and needs of older persons. To that end, AoA-supported research is aimed at developing new knowledge that will increase the capacity of State and local agencies, in both the public and private sectors, to assist older

persons in achieving and maintaining ecomomic and personal independence. AoA-funded demonstration projects seek to test new models, systems and approaches for planning and organizing effective, comprehensive services delivery systems.

Several of the AoA National Goals for FY 1990 constitute the organizing framework for describing AoA's research and demonstration initiatives in FY 1989. These goals are:

- o Older Persons as a Resource
- o Strengthening the Family and Intergenerational Bonding
- o Prevention and Alternatives to Institutional Care
- o Promotion and Enhancement of Effective Community Based Service Systems
- o Targetting - Strategic Resource Allocation

New and continuing research and demonstration project activities carried out in FY 1989 are highlighted below. They are arrayed under each of the five (5) AoA national goals and grouped according to specific focus areas.

1. Older Persons as a Resource

A. Employment/Income Generation Projects

Ongoing Project Activities: Activities continue on a project that focuses on sensitizing management and labor to the various methods that exist to increase employment and retention opportunities for older workers. The grantee is also looking at the different retirement planning services available at up to ten (10) corporations participating in the project.

An award for continued funding of a project was made by AoA to a national organization to support activities aimed at transferring innovative, international, income generating services to the United States. A major publication is being written synthesizing state-of-the-art information, models and

strategies related to small enterprise development and the special needs of older workers. Additional efforts are being made to disseminate information about income-generating enterprises for the elderly.

2. Strengthening the Family and Intergererational Bonding

A. Alzheimer's Disease Program Activities

Ongoing Project Activities: During FY 1989 work continued on a conference program jointly undertaken by AoA and the National Institute on Aging (NIA). These state-of-the-art conferences provide training and information about current practices in caregiving support for families of Alzheimer's Disease patients The program, funded by AoA, supports eight (8) NIA-sponsored Alzheimer's Disease Research Centers (ADRC's) to develop and implement fourteen (14) conferences that are targeted to State and Area Agencies on Aging, aging services providers, primary care and geriatric physicians, researchers, nurses, social workers, case managers, planners, and policy makers.

AoA, in collaboration with the Robert Wood Johnson Foundation (RWJF) and the Alzheimer's Association, Inc., (AAI) are jointly sponsoring the Dementia Care and Respite Services Program. This national undertaking is designed to demonstrate that non-profit day centers can provide financially viable day programs and other respite and health-related services needed by people with dementia and their caregivers. The program consists of nineteen (19) RWJF funded projects, nine (9) of which are co-funded with AoA and nine(9) that are co-funded with AAI.

Increasing State Agency on Aging Leadership Capacity to Assist Alzheimer's Disease Victims and Their Families

Ongoing Project Activities: Continuing their AoA project activities, four (4) State Agencies on Aging are increasing their leadership capacity for making technical support and expert training available to organizations in the State that serve Alzheimer's Disease victims and their families.

3. Prevention and Alternatives to Institutional Care

A. Housing and Supportive Services

Ongoing Project Activities: Third and final year continuation awards were made to four (4) projects funded in conjunction with the Robert Wood Johnson Foundation. These projects are designed to assist low-income elderly residents of public housing to purchase supportive services. Each project continued to provide supportive services and develop mechanisms for organizing and financing these services so they can eventually become self-supporting.

B. Quality Assurance for In-Home Supportive Services

Ongoing Project Activities: There has been a rapid increase in the need for and use of home care services by our aging society. The recent proliferation of providers, however, has heightened concern about the quality of care and the well-being and safety of older persons. To demonstrate ways of assuring higher standards of quality of in-home supportive services for older people AoA has made continuation awards to ten (10) State Agencies on Aging to develop and demonstrate model quality assurance systems. Some salient elements of these models are: intermediate sanctions to address substandard providers; consumer education and consumer feedback; regulatory requirements, licensure/sanctions; focus on prevention; use of long term care ombudsmen; use of volunteers as mediators; and self-advocacy.

4. Promotion and Enhancement of Effective Community Based Service Systems

A. Community Systems Development Efforts

New Project Activities: Four (4) grant awards were made to State Agencies on Aging to encourage and support efforts to build responsive community based systems for older persons. Each State agency is focusing on one or more unmet service needs particularly critical to the older population of the State. The effort at both the State and local levels focuses on collaboration with other State and local

agencies. One State is developing models for community focal points in rural areas while another is initiating programs to recruit, train, and retain long term care workers. A third project is focusing on the development of a community based adult day care program where currently no such program exists in the State. A fourth grantee is looking at solutions to the problem of broadening access to health care in a rural State.

B. Field Initiated Research And Demonstrations On Community Based Systems of Care

New Project Activities: Under the FY 1989 Discretionary Funds Program AoA made two (2) awards to promote more effective community based care to older persons. One project will determine the efficacy of using rural hospitals as community focal organizations working in conjunction with AAA's and senior centers to coordinate health and social services to older persons. The second project will demonstrate the efficacy of a state-wide health promotion campaign to prevent and treat diabetic retinopathy, particularly among high risk older populations.

Ongoing Project Activities: In FY 1989 AoA made six (6) continuation awards to projects that are developing an information and knowledge base on community based service systems. These research projects are analyzing current examples of planning and decision-making to determine those models which have been effective in developing comprehensive and coordinated systems of services for older persons. As a result, aging agencies at both the State and community levels should better understand what resources and abilities are required to exercise their leadership responsibilities.

Three (3) projects are employing different approaches and looking at different communities in assessing models for organizing and implementing community based systems of care. A fourth project is comparing and contrasting alternative methods of staffing and providing services to victims of elder abuse. Another project is examining models of State level long term care insurance programs, including a determination of whether it is feasible to include coverage for home and community care services.

The sixth project is using site visits, interviews, and case study analyses to develop a guidebook that will identify and discuss the critical stages of development of community based systems of care for use by States and localities.

C. State Agency on Aging Leadership Roles for Elderly Housing

Ongoing Project Activities: Three State Agencies on Aging received a second year continuation grant to continue efforts to demonstrate effective models for State agency leadership in the housing area. State agencies are working at the State level to influence State actions. At the local level they are assisting their Area Agencies on Aging to develop comprehensive community based housing plans in several communities across the State.

D. Legal Assistance For Older Persons

Ongoing Project Activities: Legal assistance is an important means whereby older persons gain access to the range of opportunities and benefits available through their community service systems. AoA made continuation awards to six (6) organizations to provide national support to State and Area Agencies on Aging, legal services developers, and legal assistance providers for older persons. These projects are designed to make legal assistance more available to older persons, especially those with the greatest economic and social needs, and to coordinate legal assistance programs with the supportive services provided under Title III of the Older Americans Act. The grantees provide substantive case consultation and training in areas of the law of special importance to older persons. By funding these national legal assistance support projects, AoA helps to ensure that lawyers, paralegals, and others have the resources available to provide effective, high quality legal assistance to older persons in need.

Four State Agencies on Aging received awards to continue project activities concerned with the expansion or improvement of the delivery of legal assistance to older individuals. Two projects demonstrate the use of less restrictive alternatives in guardianship cases. The third project tests the feasibility of delivering legal assistance to homebound, rural older persons through a network of volunteer seniors and pro bono attorneys.

The fourth project employs a needs assessment to improve its statewide system of using lay advocates in each county aging unit to provide legal assistance to older persons.

5. Targetting - Strategic Resource Allocation

A. Alternatives To Guardianship

New Project Activities: In FY 1989 AoA made grant awards to three (3) new projects that are designed to encourage further development of alternatives to guardianship. One project will demonstrate a model of early intervention services for older persons in three (3) communities. This model will include: representee payee services; bill payer services; and the development of self-help materials on money management. A second project is developing a national training module on guardianship alternatives and support services for the aging network, including providers of aging, legal, social, and adult protective services. This module is being tested in three (3) States. The third project is developing a knowledge base about guardianship systems through a national survey of State practices in such areas as assignment and provision of guardianship services and the characteristics of adults affected by guardianship.

B. Developing Minority Elderly Agendas in National Organizations

New Project Activities: In FY 1989 AoA made five (5) awards to national organizations to develop or enhance their own knowledge of minority aging issues and to broaden their capacity to deal with the concerns of low income minority elderly on an on-going basis. In addition, these organizations are conducting the following activities: (1) creating a national network of Hispanic community-based groups committed to serving the elderly; (2) undertaking collaborative efforts between two national organizations, one of which serves the Black elderly, to develop local programs for the Black elderly using the resources of both organizations; (3) developing

support, on a national level, to expand research initiatives focused on issues concerning minority elderly; (4) supporting State Minority Task Forces through training and technical assistance; (5) encouraging national organizations representing components of State governments to address minority elderly issues and; (6) training minority professionals to become leaders in the field of aging. An additional award was made to a national organization to support its efforts to be responsive to the needs of elderly Pacific/Asians.

Ongoing Project Activities: Three (3) national minority organizations addressing the interests of the Hispanic, Black, and Native American communities continued their AoA project activities in FY 1989. A significant part of these activities are focused on mobilizing community resources to provide a continuum of care for vulnerable older persons and to help them live as independently as possible.

C. Studies on Alcohol Abuse and Alcoholism Among the Aged

New Project activities: In FY 1989 AoA funded two (2) new projects to develop a knowledge base about the incidence and prevalence of alcoholism and alcohol-related problems among older people. Research activities include collection of data on such factors as drinking patterns, psychosocial behaviors, family relationships, life satisfactions, home environments, health, financial issues, and personal values. Outcomes of these projects will help State and local governments plan future programs focused on prevention, detection, and treatment of alcoholism among their older citizens. In addition, one of the projects is developing a computerized data base so that researchers will be able to investigate various issues related to alcohol-related problems among the Black elderly.

D. Research On Native American Aging

Ongoing Project Activities: Five (5) grantees continue their project activities designed to develop a knowledge base that will give AoA, and other appropriate organizations, a clearer understanding of the needs of older Native Americans and Native Hawaiians. These activities will also provide insight into how resources can be better targeted to these minority aging

populations. Data are being collected on such factors as demographics; health, housing, and socio-economic conditions; and the availability and accessability of supportive services.

E. National Aging Resource Center on Elder Abuse

Ongoing Project Activities: The National Aging Resource Center on Elder Abuse (NARCEA) is led by the American Public Welfare Association working in collaboration with the University of Delaware and the National Association of State Units on Aging. Established in FY 1989, NARCEA serves as a resource of information, data, and technical expertise on elder abuse to State and local aging and adult protective service personnel, to other professionals and practitioners concerned with elder abuse, and to the public.

During its first year, NARCEA conducted informational and technical assistance workshops at nine conferences involving professional groups, aging and protective service agencies, and organizations representing service providers working in the field of elder abuse. The Center organized teleconferences in which eighty State Aging and Adult Protective Services personnel, representing thirty-three States, participated to identify training and technical assistance needs and existing resources. As a result, NARCEA published a report of the ten priority training and technical assistance needs identified thru the teleconferences and followed up with four Technical Assistance Memoranda to State Aging and Adult Protective Services Offices. In addition, the Center has developed a file which identifies, by State, resources such as training curricula, research findings, videos, and persons recognized to be experts in specific aspects of elder abuse research, training, and services.

NARCEA's principal mechanisms for information dissemination are NARCEA EXCHANGE, a quarterly newsletter, and the Clearinghouse on Abuse and Neglect of the Elderly (CANE). Three issues of NARCEA EXCHANGE were disseminated free of charge to 2,600 persons located in all fifty States, the District of Columbia, and the U.S. territories. CANE generated customized annotated bibliographies and filled requests for publications.

NARCEA concentrated its first year research efforts on developing a report which analyzes State elder abuse incidence data for the years 1986 thru to 1988.

F. National Resource Center on Minority Aging Populations

Ongoing Project Activities: The National Resource Center on Minority Aging Populations was established in FY 1989 as a collaborative effort between San Diego State University and the University of Southern California. The Center was established to serve as a national focal point for techical assistance, training, information dissemination, and short-term research. Its efforts are supporting States, communities, educational institutions, professionals in the field, and the public in understanding and responding to issues affecting minority elderly.

During FY 1989, the Center queried all States for their technical assistance and training needs and presented numerous workshops on a variety of minority aging issues. It developed a registry of resources for minority aging populations and created a computerized clearinghouse on minority aging. The Center began publication of a bi-monthly newsletter, The Minority Aging Exchange. It published a Mini-Report on Targeting in the Older American Act and revised a previously written manual, "Enhancing Services to Minority Elderly Training Manual". The Center is responding to ad hoc technical assistance requests from State Agencies on Aging on a variety of issues related to minority elderly.

G. National Resource Center for Rural Elderly

Ongoing Project Activities: The National Resource Center for Rural Elderly was established in FY 1989 at the University of Missouri at Kansas City. Its technical assistance, training, information dissemination, and short-term research efforts are supporting States, communities, educational institutions, professionals in the field, and the public in understanding and responding to issues affecting the rural elderly.

The Center is serving as a national focal point for the identification of best-practice programs and services for the rural elderly in three primary focus areas (access/transportation, health/care coordination, andhousing/assisted living alternatives). The

Center conducted workshops in the areas of access/transportation and needs assessments and also developed manuals in these areas for dissemination early in FY 1990.

The Center is publishing a bi-monthly newsletter and developed and disseminated a "Rural Elderly Bibliography." The Center is responding to ad hoc technical assistance requests from State Agencies on Aging on a variety of issues related to the rural elderly.

o Evaluation

Section 206 of the Older Americans Act authorizes evaluation of the impact of programs funded under the Act, including their effectiveness in achieving stated goals. AoA's evaluation program in FY 1989 included the finalization of one project.

This evaluation, entitled "A Short Term Evaluation of the Visibility of Aging Services Systems at the Local Level", studied the strategies for increasing the visibility of aging services at the local level. The overall purpose of this study was to identify successful efforts that have been undertaken to increase public awareness, knowledge, and understanding of aging services at the local level.

The project also examined how these efforts have been implemented, characteristics of State and Area Agencies conducting these activities, State and Area Agencies' efforts to strengthen ties among services for older persons, and the impact of increased public awareness on the system of aging services within the community. The results of this evaluation are being considered by AoA as it develops initiatives in fulfilling AoA's goals and objectives.

Administration on Aging

Alzheimer's Disease

In FY 1989, the Administration on Aging (AoA) maintained a number of activities designed to develop and strengthen community based care for the victims of Alzheimer's Disease (AD) and their families. These activities included: AoA/NIA co-sponsored state-of-the-art conferences that focused on current practices in caregiving support for families of AD patients; collaborative efforts involving AoA, the Robert Wood Johnson Foundation (RWJF) and the Alzheimer's Association that supported a number of demonstrations in the RWJF Dementia Care and Respite Services Program; and projects designed to demonstrate better ways to provide community care for people with AD as well as their family caregivers.

AoA also continued its support of a National Long Term Care Resource Center with a focus on Alzheimer's Disease and other dementias. The Center is specifically devoted to providing training, technical assistance, short-term research, and dissemination activities for State Agencies on Aging, and others, in AD and other dementias. The Center continues to focus its assistance efforts on developing effective service programs to deal with the problems of short-term treatment and long-term management of AD patients and with the needs of family caregivers. AoA plans to continue its support of this center in FY 1990.

AoA is also planning on including a priority area that addresses AD in its FY 1990 Discretionary Funds Program. Grant applications will be solicited to develop projects that demonstrate ways to improve access to services by minority persons with AD and their family caregivers.

Public Health Service

AGENCY FOR HEALTH CARE POLICY AND RESEARCH

Formerly the
National Center for Health Services Research
and Health Care Technology Assessment

AGING

The Agency for Health Care Policy and Research (AHCPR) was established on December 19, 1989 as a separate Public Health Service (PHS) agency by the Omnibus Budget Reconciliation Act of 1989, P.L. 101-239. As authorized under a new Title IX of the PHS Act, the purpose of the agency is to enhance the quality, appropriateness, and effectiveness of health care services and to improve access to such services. This will be accomplished through the establishment of a broad base of scientific research and through the promotion of improvements in clinical practice and in the organization, financing, and delivery of health care services. The new agency replaces the former National Center for Health Services Research and Health Care Technology Assessment.

As the leader of Federal efforts in outcomes research and health services research, the AHCPR seeks to create and disseminate new knowledge and better understanding of the processes by which health services are made available and how they may be provided more efficiently and effectively. The AHCPR conducts and supports scientific research that tests the assumptions on which current health policies and practices are based, assesses the performance of the health care system, and examines alternate ways to organize, finance, and deliver health services. AHCPR's program is directed towards the needs of health care policymakers, providers, and consumers. It addresses the full array of health care issues, among them long term care and health services for the aging.

With the aging of the population, the technical advances in medical care, increased survival among both the young and the old, and the prospect of a widespread epidemic of AIDS, the availability, costs, and financing of long term care services are major issues in public policy. The problem in this area will increase as more diagnostic and therapeutic innovations prolong life. The country now spends in excess of $40.0 billion for patients with Alzheimer's disease and related dementias. The costs for caring for patients with dementia associated with AIDS may dwarf these expenditures. Yet, despite the current and anticipated growth in expenditures for long term care, relatively small sums have been available to study how these services might be delivered more effectively and efficiently.

The goal of the AHCPR health services research program in long term care and health services for the aging is to develop alternative strategies for providing long term care that will reduce Federal expenditures for these services, increase their availability, and improve their quality. In FY 1990-FY 1991,

AHCPR will undertake a number of initiatives to expand research on aging and long term care. Studies of home health care and the role of caregivers will be included in both the AHCPR intramural and extramural programs. AHCPR also will support studies that address a variety of questions on the economics of health care and the elderly.

Medical Treatment Effectiveness/Outcomes Research

Studies supported by the Agency for Health Care Policy and Research (AHCPR, formerly NCHSR) over the past 15 years show that there are often wide variations in tha types of health care furnished to apparently similar populations within and across geographic areas. Of even more concern, the research also shows that often these variations are associated with different outcomes.

The Medical Treatment Effectiveness Program (MEDTEP) of AHCPR has significance for saving and extending lives, improving the quality of health care for Medicare beneficiaries and other patients, increasing and maintaining patients' functional abilities, and conserving resources. These benefits can occur as a result of new investment in the development and dissemination of scientific knowledge about patient outcomes, allowing health care providers and their patients to make more informed decisions about treatment options.

Health services research in this country and elsewhere indicates that variations in the use of health care services and procedures reflect the complex interaction of clinical, social, environmental, economic, and psychological factors that shape the relationship between patient and provider. Variations are appropriate if they arise from differences in the needs and choices of individual patients, and if the alternative patterns of care are known to be equally effective and efficient. However, the "practice styles" of physicians account for many of the differences observed in the care of patients with similar conditions, and providing physicians with information about the outcomes of care reduces these variations considerably. Practice styles are most variable for those health care conditions and procedures associated with greatest uncertainty and controversy among physicians. Research on patient outcomes and the dissemination of its findings will help to reduce these uncertainties and resolve these controversies.

Under the aegis of the AHCPR, the Medical Effectiveness Treatment Program will rely heavily on the complementary activities and unique contributions of other agencies of the Public Health Service and the Health Care Financing Administration.

MEDTEP involves four sets of activities: health services research on outcomes, effectiveness, and appropriateness of health care services and procedures; database development;

dissemination of research findings; and guidelines development. The research component of MEDTEP is the responsibility of the Center for Medical Effectiveness Research (CMER) in the AHCPR and encompasses the first three activities: effectiveness and outcomes research, database development, and research on the most effective ways to disseminate the findings.

In FY 1988, the former National Center for Health Services Research and Health Care Technology Assessment (NCHSR) initiated the first stage of the Medical Effectiveness Treatment Program (MEDTEP). An extramural research program on the impact of medical practices on patient outcome was established. This program built on NCHSR's long history of support for patient outcome research, including the pioneering work of J.E. Wennberg, M.D., of Dartmouth Medical School.

Highlights of 15 years of NCHSR-supported outcomes research include:

- In the early 1970s, Dr. Wennberg reported wide variation in the numbers of tonsillectomies performed by physicians on similar patients, even within small and apparently similar communities in Vermont. Children in the areas with low rates of tonsillectomies did not appear to experience adverse health outcomes (Wennberg, et al., Science, 1973).

- A comparison of surgery and hospitalization rates in Boston and New Haven indicated that a resident of New Haven was about twice as likely to undergo coronary artery bypass surgery as a resident of Boston. The rates of knee and hip replacements were higher in Boston while substantially higher rates of hysterectomy and back surgery were found in New Haven (Wennberg, et al., The Lancet, May 23, 1987).

- Analysis of Medicare population-based rates for 153 diagnostic and surgical procedures in 13 regions revealed large variations. Over half of the procedures, including coronary artery bypass surgery, showed a more than three-fold variation among regions. A few procedures, including hernia repair and appendectomy, showed relatively little variation (Rand, The New England Journal of Medicine, 1986).

- Comparison of Boston and New Haven revealed that per capita medical care costs were 50 percent lower in New Haven. A saving of $300 million in hospital expenditure would be possible if the New Haven costs were extrapolated to Boston (Wennberg, et al., The Lancet, May 23, 1987).

- An assessment of prostatectomy and its alternative, "watchful waiting," for the treatment of prostatic

hypertrophy, was carried out by the Maine Medical Association. This assessment determined that the frequently performed surgical procedure was neither as beneficial nor benign as generally thought. Only slightly more than half the surgical patients experience a fully satisfactory result. The study recommended that the patient be more fully informed of the benefits and risks and that patient preferences dominate the decision regarding prostatectomy versus waiting (Wennberg, et al., Journal of the American Medical Association, May 27, 1988).

- An international analysis of mortality and reoperation after open and transurethral prostatectomy (TURP) of the prostate for benign prostatic hyperplasia found that TURP was less effective in overcoming urinary obstruction than the open operation. TURP may also result in increased long-term risk of death. A prospective clinical study was recommended for further examination of this relative risk (Roos, et al., The New England Journal of Medicine, 1989).

- A comparison was made of the rates of hospital use and mortality among Medicare enrollees in Boston and New Haven. Adjusted rates of discharge, readmission, length of stay, and reimbursement were higher in Boston. High-variation medical conditions accounted for most of the differences. However, the lower rate of hospital use by Medicare enrollees in New Haven was not associated with a higher mortality rate (Wennberg, et al., The New England Journal of Medicine, October 26, 1989).

FY 1989 marked a significant expansion in the AHCPR effort to develop reliable and comprehensive data on the effectiveness of different medical treatments. Four research teams were funded under the Patient Outcome Assessment Research Program (POARP). The POARP was authorized by the Omnibus Reconciliation Act of 1986 and reauthorized by the Technical and Miscellaneous Revenue Act of 1988, transferring monies from the Medicare Trust Fund for the support of outcomes research.

The four teams include both community and academic physicians. Each team is to identify and analyze the outcomes of alternative practice patterns. Researchers will assess comparative effects of alternative therapies on patient survival, quality of life, costs, and other factors. The teams will develop and test methods to reduce inappropriate variations in the treatment of conditions that affect a large number of Americans every year: low back pain, heart attacks, cataracts, and prostate gland enlargement.

In awarding these POARP grants, priority was given to research on medical and surgical illnesses for which intervention

poses a high risk or offers a high potential benefit to the patient, or for which data indicate a highly variable pattern of provider practices within or among distinct geographic areas, or where the interventions are significant in terms of utilization, length of hospital stay, or cost.

Specifically, grant awards were made in FY 1989 to the following projects, which are expected to require about 5 years to complete:

-- Richard Deyo, M.D., University of Washington, Seattle, will assess nonsurgical interventions for low back pain and different types of lumbar spine surgery for back problems, especially for spinal stenosis, the leading cause of back pain hospitalization among the elderly. Although not fatal, low back pain sends more Americans to see the doctor than almost any other disorder. Approximately 80 percent of all adults suffer from low back pain at some point in life. The research also involves the Maine Medical Assessment Foundation of Manchester, ME.

-- Barbara J. McNeil, M.D., Harvard Medical School, Boston, MA, will establish a national database of information about patient outcomes from the use of alternative treatments for myocardial infarction, which strikes more than 250,000 Medicare beneficiaries every year. Their cumulative mortality rate is 40 percent.

-- Earl P. Steinberg, M.D., Johns Hopkins University, Baltimore, MD, will assess three different procedures for the treatment of cataracts. Over 1 million cataract operations are performed on Medicare beneficiaries annually, making it the most common surgical procedure for this population.

-- John E. Wennberg, M.D., Dartmouth Medical School, Hanover, NH, will assess transurethral resection, open prostate surgery, and nonsurgical interventions for enlargement of the prostate gland, as well as radical surgery and other therapies for localized cancer of the prostate. Enlargement of the prostate affects 8 out of every 10 men by the time they reach 80 years of age.

In addition, AHCPR awarded grants in FY 1989 to seven additional patient outcome assessment teams to assist them in planning for evaluation of the management of peripheral vascular disease, cerebral vascular disease, hip disease, colon cancer, gall bladder disease, and coronary artery disease.

In FY 1990, the new agency, the Agency for Health Care Policy and Research (AHCPR), was created by P.L. 101-239 to have primary responsibility for the implementation of MEDTEP. Building on the past efforts of the former NCHSR, this new agency

is to undertake a broadly based research and dissemination effort through collaborative activities with other agencies of the Public Health Service (PHS) and the Health Care Financing Administration (HCFA).

MEDTEP's purpose is to improve the effectiveness and appropriateness of health care services and procedures through better understanding of the effects of health care practices on patient outcomes. The central questions of this new program are:

- What treatments work best?
- Has the patient's functional status improved?

Extramural Research

The AHCPR extramural research program is carried out through peer-reviewed grants and contracts conducted at universities, at nonprofit organizations and institutions such as teaching hospitals, and by industry. In Fiscal Year 1989, a number of extramural research projects on issues related to developments in aging, the elderly and long term care were supported.

Projects Completed in FY 1989:

"Conference on Medicare and Research"
Mark Pauly, Ph.D., University of Pennsylvania, Grant No. HS05680

The Medicare conference held in October 1986 highlighted, through the delivery of invited papers and panel discussion, findings and issues dealing with Medicare and its effects on utilization, provider choice, and financing. The conference proceedings, entitled Lessons from the First Twenty Years of Medicare: Implications for Public and Private Sector Policy, was published in January 1989 by the University of Pennsylvania Press. Copies are available from University of Pennsylvania Press at $34.95. Further information on the publication was included in NCHSR Research Activities, February 1989.

"Impact of DRGs on Public Home Health Nursing Services"
Elayne K. Phillips, Ph.D., University of Virginia, Grant No. HS05513

To study the impact of hospital prospective payment on the consumption of home health nursing resources. This study focused primarily on the changes in resource utilization in public home health since hospital implementation of the prospective payment system (PPS) by Diagnostic Related Groups (DRGs). Although the institution

of DRGs was limited to Medicare recipients in hospital settings, preliminary reports suggested that changes in practice patterns were not limited to this population. Hospital patients were experiencing shorter lengths of hospital stay after prospective payment by DRGs and were discharged in less healthy states. Although providers had consistently reported shifts to more complex patients in home health patient populations, these changes had not been documented empirically. To begin this process, the current study investigated changes in requests for care and care delivered to public home health patients as related to the implementation of prospective payment by DRGs.

Two major research hypotheses were tested. First, that public home health nursing resource consumption would increase from the pre-DRG period to the post-DRG period. Second, that the increase in Medicare patients would be greater that non-Medicare patients. Twenty percent of all home health patients were randomly selected from health department home health patient referral logs across Virginia. This resulted in approximately 2,000 cases. Referral and billing forms were reviewed by registered nurses. Resource measures included frequency and number of nursing services requested, number and hours of billed visits delivered, and length of patient care episode. Analyses compared all groups pre- to post-DRG, and compared Medicare to non-Medicare groups. A subsample of approximately 300 Medicare cases was selected for additional study. Record reviews provided data on household composition, total nursing visits (billed and unbilled visits), and other nurse contacts, including telephone calls, conferences, and care related trips.

The following findings were reported: [1] The implementation of prospective payment by DRGs in hospitals was found to be associated with a significant increase in demand for home care. [2] Significant differences were found between Medicare and non-Medicare patients in the utilization of home health resources and in outcome. [3] Variation in local area characteristics accounted for differences in resource consumption across agencies. [4] Analysis of the subsample revealed that on the average 1.5 unbilled nursing visits and 10 nursing contacts were made per episode, seven of which were telephone calls.

Conclusions are as follows: Public home health patients had more services requested after the implementation of hospital prospective payment by DRGs and these needs increased at a faster rate than did services delivered. Medicare home health patients did not appear to be selectively affected by the implementation of hospital prospective payment. In fact, the entire system was much more stable than anticipated.

Nevertheless, absolute differences in services requested and delivered ere observed between Medicare and non-Medicare groups and between older non-Medicare and Medicare patients. Non-Medicare patients received more frequent, intense acute care, while Medicare patients received more intermittent, extended, chronic care. Among older patients, both Medicare and non-Medicare, needs for care were fairly uniform, reflecting a chronic, frail population. Older non-Medicare patients, who frequently had no ability to pay for care, received more aide visits and had more favorable outcomes.

The significant amount of heterogeneity existing across the state in requests for and delivery of care suggests that the community need for home health services cannot simply be determined by population size. Similarly, patient-level resource needs vary tremendously. Identification of high-risk communities and patients can be facilitated based on specific characteristics identified in this study.

The present amount of unbilled care delivered consumes a large amount of agency resources. The study suggests that unbilled care is an integral part of the structure and delivery of home health care. In the future, this care is likely to decrease due to agency pressure on staff to maximize reimbursable care. This component could be crucial to outcomes and deserves further study

The principal investigator developed recommendations for research, administration, education and policy development based on the findings and conclusions. This material will be reported on more fully in the literature.

"The Use of Medical Services and the Decision to Retire"
Charlotte Muller, Ph.D., Research Foundation, CUNY, Grant No. HS05729

To determine whether self-assessed poor health status is a rationalization or a reason for early retirement, this study compares health status of males reported before and after retirement in analyzing the relationship between the decision to retire and early death and between the decision to retire and the demand for medical care. The results show that the probability of dying within two years after retiring and the probability of seeking medical care at the time of retirement are much higher for retirees with health problems and especially for those retirees who report health problems and retire before 65. Work-limiting health problems, though self-reported are a reason for retirement. These findings are of importance given current policy to increase the retirement age. The results of this study are scheduled for publication in Health Services Research in the

Spring of 1990. An AHCPR Research Activities Statement is in preparation for publication in 1990.

"Study of Chain Nursing Home Case-mix, and Staffing"
John Holahan, Ph.D., The Urban Institute, Grant No. HS05253

This grant originally looked at the effect of chain controlled nursing homes on cost, quality and access to long term care. However, the focus (but not the title) has changed to the effect of the Prospective Payment System (PPS) on access to nursing homes for Medicare patients, using data before and after implementation of PPS. The analysis is based on several separate but related analyses designed to examine different aspects of the access issue.

Although utilization of Skilled Nursing Facility (SNF) case increased between 1983 and 1985 as hospitals were being phased into the Medicare PPS system, Medicare covered SNF admissions declined. This finding indicates that increases in utilization of nursing home care by Medicare patients of SNFs were covered by other payers.

Results indicate that severity of the casemix of patients treated in Medicare SNFs increased over the 1983-85 period as hospitals were being phased into the Medicare PPS system. PPS appears to result in the discharge of a patient mix that requires greater SNF resources in PPS-covered states than in waiver states.

Medicare-covered SNF patients are considerably more costly to nursing homes than non-Medicare patients with the average cost of a Medicare-covered day in SNF-only facilities almost twice as high as a private inpatient day.

"Prospects for Caring for Persons with AIDS in Nursing Homes"
Rosalie Kane, University of Minnesota, Contract No. 282-87-0049

PWAs differ from a typical nursing home population in age, gender, stigmatized lifestyle, infectious nature of their disease, and need for complex medical care. To date, little systematic effort has been made to tap the perspective of those who live and work in nursing home, particularly the former.

In this study original data was collected from 100 nursing home residents, 100 nursing home responsible family members, and 100 nursing home direct care staff (N-300) in 16 Minnesota nursing homes, 8 of which were known to be willing to accept PWAs and a matched group that had not indicated such an intention. For the 3 samples, the investigators studied knowledge about and attitudes towards

AIDS, and compared these to National Center for Health Statistics (NCHS) data about the general public. They also conducted detailed interviews with a small number of PWAs (N=4) about their nursing home experiences, and interviewed the administrators, directors of nursing, and directors of social work in the 16 homes (N=48) to further explore factors associated with the decision to treat PWAs in nursing homes and the experiences of facilities that did. These data were augmented by a literature review and a case study of expert opinion in the state and nationally.

Preliminary findings suggest that nursing home residents are somewhat less informed about AIDS than the general public, that nursing home residents' family members are similar in knowledge to the general public, and that nursing home staff (50 certified nursing assistants, 25 LVNs, and 25 RNs) are somewhat better informed than the general public. On the other hand, substantial misinformation and apprehension about AIDS exists in all three groups. With some exceptions, there were few differences in knowledge and attitudes in respondents associated with the 8 homes that were willing to serve PWAs compared to respondents associated with the comparison group facilities. In all categories, significantly more respondents in the homes that admitted PWAs stated they had met a PWA, but many of the residents and families in homes admitting PWA were unaware of the facility's policies.

Some, but not all line staff express fear of contagion, a fear also echoed by residents and family members. Some, but by no means all, residents expressed negative attitudes toward gays and drug abusers. In all categories interviewed, those who indicated they knew a PWA were more positive and knowledgeable than those who did not. The PWAs interviewed expressed a wide range of negative reactions to the nursing homes environment, and respondents in all categories suggested possible changes to make the nursing home more conducive to caring for PWAs. Considerable support was expressed for special nursing home units for PWAs.

Concerns of nursing home executive staff regarding care for PWAs were similar to those found in the literature reviewed. They included 1) inability to meet physical needs of PWAs, 2) inability to meet psychological and social needs of PWAs; (3) concerns about cost of care and inadequate 3rd party reimbursement; (4) concerns about a negative reaction from geriatric clientele; and (5) legal concerns.

Projects Ongoing in Fiscal Year 1989:

"Variations in Patterns of Primary Care Among the Elderly"
Charlyn D. Black, M.D., Johns Hopkins University, Grant No. HS06099.

This dissertation research grant is a retrospective analysis of existing research data derived from 1) claims data from a provincial health insurance program, (the Manitoba Health Services Commission) and 2) survey responses that have been linked to claims data for elderly individuals (The Manitoba Longitudinal Study on Aging). Ambulatory claims will be used to operationalize four important attributes of primary care: first contact care, comprehensiveness, coordination, and longitudinality. The measures will be validated by examining relationships between the four measures, and be comparing scores for these attributes with survey responses that capture individuals' assessment about these aspects of their general medical care. Correlational and inferential analyses will be used in the analyses. The four attributes of primary care will be assessed by examining the degree to which age, sex, health status, educational, and monthly income explain variation.

Achievement of the objects may contribute to fostering more useful and credible research on the impact of primary care. The potential to quantify patterns of primary care allows linking information about variations in patterns of primary care with cost and effectiveness data, and to advance our understanding of the impact of primary care.

"The Use of Durable Power of Attorney in the Nursing Home"
Jiska Cohen-Mansfield, Ph.D., Hebrew Home of Greater Washington, Grant No. HS06090

This small grant examined the preferences of elderly nursing home residents regarding the health-care decision-making process. It investigated: (1) Preferences for the choice of an agent for health-care, decision-making; (2) preferences for future life sustaining treatment; and (3) factors that might have influenced their preferences, such as previous experience with life sustaining treatments, religious beliefs, and personal values.

One hundred three residents of a large suburban Jewish nursing home participated in the study. Each participant was interviewed and several close-ended questionnaires were administered. In the interview, residents indicated the identity of their preferred decision-maker for health care and decided whether to formally execute a durable power of attorney. In the Preferences for Life-Sustaining Treatments Questionnaire, participants reported their preferences for

or against four life sustaining treatments under three hypothetical levels of future cognitive functioning.

Results showed that participants tended to choose a son or daughter as their agent for future health-care decision-making. In most cases, this person was their closest relative. Subjects had clear and consistent patterns of preferences regarding the utilization of life-sustaining treatment. Generally, subjects would not opt for treatment. They were less inclined to opt for treatment as their future level of cognitive functioning declined, or when the anticipated treatment was applied on a permanent rather than a temporary basis.

"Practice Variation in Care of Arthritis"
Curtis Henke, Ph.D., Institute for Health Policy Studies, Grant No. HS05912

This study will use existing data from an ongoing longitudinal survey to examine variation among rheumatologists in their use of medical and surgical hospitalizations as a part of the treatment of patients with rheumatoid arthritis. The specific aims are to: [1] measure variation in the observed hospitalization rates and the extent to which it is related to differences in the medical, functional, and socio-economic characteristics of rheumatoid arthritis patients and to the incentives of the physician's practice; [2] estimate parameters representing each rheumatologist's individual practice style in decisions to hospitalize; [3] measure the stability of practice styles and overall practice variation from year to year; [4] estimate the relationship of practice styles to training and practice characteristics; and, [5] determine whether differences in practice style are associated with differences in total treatment costs and patients' functional outcomes.

This study will have an impact on the clinical management of rheumatoid arthritis (RA). While it focuses only on hospitalization and surgery as outcome measures, the findings could help in the design of a more comprehensive study of RA therapy. The results should provide important insight and could serve as a model for confirmatory studies in other settings.

"Case Control Study of Aged Users and Non-users of Home Health Care"
David Rabin, M.D., Georgetown University, Grant No. HS06049

This study will determine whether persons over age 60 who use home health care services differ significantly from non-users, in terms of functional status, spousal and social support, and sociodemographic characteristics. Data from

the 1984 Supplement on Aging to the National Health Interview Survey will be analyzed using a case control methodology to compare those reporting use of home health care services (e.g. visiting nurses, home health aids), with those reporting use of other community services (e.g. meals on wheels) and no community services use.

Home health care is becoming an issue with major policy implications. While the majority of care has been provided in the past by informal caregivers (family and friends), with the increase in the aged population and concomitant aged potential caregivers, this will place a greater demand on the formal care providers (home health agencies). This study will provide insight on changes by informal care providers between the analysis of the 1982 Long Term Care Survey by NCHSR Intramural Researcher Robyn Stone ("Exploding the Myths: Caregiving in America") and the 1984 Health Interview Surveys. It will also provide a basis for interpreting the 1988 National Medical Expenditure Survey (NMES) Home Health Component that does not specifically address home visits by nurses.

"Effects of Advance Directives in Medical Care"
Lawrence Schneiderman, M.D., University of California at San Diego, Grant No. HS05617

The effects of an advance directive will be determined by a longitudinal, randomized experiment of 100 experimental and 100 control subjects all of whom have life-threatening illnesses. The experimental subjects are being offered the opportunity to execute an advance directive by their physicians; the controls do not receive an offer. All subjects are measured to determine levels of satisfaction, health status, health locus of control, utilization of health services and costs of care at intake, three months, six months, one year and tow years. Analyses will be carried out within the context of the General Health Policy model.

The study is expected to show that an advance directive will increase patient satisfaction and control, have no effect on patient's health status, and decrease cost by not using expensive life-sustaining forms of care that it is believed can have no demonstrable effect on patient health for a specific subset of terminally ill patients.

New Starts in Fiscal Year 1989:

"Impact of Toileting Dependence on Home Health Charges"
Dorothy J. Baker, Yale University, Grant No. HS06291

This dissertation research grant will retrospectively examine data already collected on a cohort of 8,000 low income elderly persons in the state of Connecticut receiving home care through a special program (Promotion of Independent Living) administered by the state's Department on Aging during the period 1982-1986. Four sources of data will be used: Medicaid and Medicare records, PIL records, nursing home admissions, and state data. Multivariate analyses will be used to examine how the following variable influence the use of services: patient activities of daily living (ADL), availability of informal social support, availability of long-term care services in the community, and use of inpatient hospital services.

This study is expected to make unique contributions to the currently rather sparse literature on determinants of use and costs of home care. The special emphasis on examining dependence in toileting is warranted by the special burdens it places on patients and on informal and formal caregivers. Despite growing recognition of the importance of this particular set of problems, previous research has only indirectly estimated its cost implications. Moreover, most evidence is based on the experience of populations residing in nursing homes. This unique data set and the results of the analyses will provide valuable insights that may influence home care policy and may help to motivate further clinical research addressing the problem of incontinence.

"Home Health and Nursing Home Market Analysis"
Charlene Harrington, University of California at San Francisco, Grant No. HS06174

Secondary data from Medicare and Medicaid and other sources and primary data to be collected on state policies and bed supply for the period 1986-1988 will ba used for this study. By building upon previous HCFA and NCHSR studies, the project will develop a ten-year cross-sectional time series data base of both secondary and primary data for 1978-88. A pooled cross-sectional time series regression analyses will be conducted to examine differences within the ten-year time period. The analyses will use both integral and dynamic equation models of the home health and nursing home markets developed by the investigators to test a series of specific hypotheses regarding the nature of the two markets.

This study will produce papers designed for policymakers to consider in making changes in Medicare and Medicaid program policies. The descriptive analysis will provide valuable new primary data on state Medicaid nursing home and home health reimbursement rates and methods and total state nursing home bed supply not available from other sources. This study will examine the trends in state spending during the ten-year time period, and examine differences in pre- and post-Omnibus Budget Reconciliation Act of 1981 (OBRA) and pre- and post-DRG periods. The analyses will develop a better understanding of the market forces, which is said to be needed by researchers, industry officials, and policymakers.

"Urban/Rural Differences in Elderly Use of Long-Term Care"
Dr. Charles McConnel, University of Texas Southwestern Medical Center, Grant No. HS06197

Dr. McConnel will establish the extent and determinants of differences in survival and utilization of health and community based services by the rural/urban elderly. Data from the Longitudinal Study of Aging, the Census of the Population, the National Death Index, and the Health Professionals Resource File will be linked. A single analysis will then link a defined population data by health status, health services access, and health services utilization. The outcome variables include: physician visits, nursing home admissions, home health and/or nursing visits, homemaker services, use of community services and hospitalization.

"Functionally-Limited Elderly Living Alone: Access to Help"
Charlotte F. Muller, Ph.D., Research Foundation, CUNY, Grant No. HS06030

This study examines whether disabled elderly living alone differ in the availability of informal care, functional limitations and economic resources from elderly living with others. Additional research questions include not only the effect of caregiving on women's employment,but also the effect of employment on the amount of time given to informal care. Data sources include the 1982 and 1984 national Long Term Care Survey.

Preliminary findings indicate full-time employment substantially decreases the time allocated to informal care. Information from this study will aid in strengthening public policies aimed at maintaining the disabled in the community.

"Living Wills for Primary Care, AIDS, and Cancer Patients"
John D. Stoeckle, Massachusetts General Hospital, Grant No. HS06120

The objective is to assess whether comprehensive living wills are practical and desired by physicians and patients, and to provide some models for how they can handle the process of indicating preferences for care, and develop a model for living will format.

Three groups of patients will be surveyed about issues pertaining to living wills. The groups are: 388 patients seen in primary care physicians' practices; 291 patients with AIDS and 410 patients from a telephone registry. The first two groups will be interviewed by their physicians during regularly scheduled office visits, while the third group will be interviewed by telephone. The survey will be re-administered after six to 12 months, as well as after any interim hospitalization. In future follow-up on the cohorts used in the proposed study (not covered by the current funding), the investigators would seek to ascertain the impact of the living will on hospital costs of terminal care.

The specific goals of this proposal are: (1) to improve the format of available predrafted living wills by allowing individuals to specify preferences based on several hypothetical scenarios (2) to assess patients' interest in discussing terminal care issues, as well as their perceptions of barriers to such discussion; (3) to assess the extent to which patients have, and wish to have, living wills; (4) to assess how durable (reliable) patients; preferences are; and (5) to measure any changes inpatients' attitude regarding living wills as a consequence of participating in the survey (by self-report).

"Measurement of Preferences for Life-Sustaining Treatment"
Richard F. Uhlmann, University of Washington, Grant No. HS06343

The objective of this project is to measure the validity and reliability of patient preferences for life-sustaining treatment and states near to or worse than death, to identify the medical interventions, and health and social states which form the domain of content for advance directives, as well as the factors which influence their acceptability.

This study has three phases. In Phase I, 50 patients, 10 well adults, 15 physicians, and 15 nurses will receive a semistructured interview to identify the relevant content for advance directives and to pretest methods for Phase II. In Phase II, 250 patients and 100 well-adults will be

administered a structured interview to scale their preferences for states and medical interventions, and evaluate the construct validity, predictive validity, and internal consistency of their preferences. In Phase III, patients and well-adults will be reinterviewed two weeks and six months following their enrollment in Phase II to evaluate the test-retest reliability and predictive validity, respectively, of their preferences. Patients will include persons with the acquired immunodeficiency syndrome, terminal illness, elderly with chronic disease, cognitively impaired, and nursing home residents. Physicians will be selected from a variety of primary care and subspecialty practices. Nurses will be selected from intensive care, inpatient, outpatient, home health, and nursing home practices.

Results will be directly applicable to the development of valid, efficacious, and effective advance care directives. In addition, they will provide an improved basis for understanding the validity and reliability of preferences contained in advance directives.

Intramural Research

The aging of the U.S. population has heightened public and private focus on the health, social, and residential services required by individuals who have lost the ability to function independently because of ill health and physical and mental impairments. The increasing risk with age of incurring such impairments, coupled with the rapid growth of the elderly, will ensure that caring for the impaired elderly will continue to be an important issue for public and private policies.

The AHCPR intramural research program directly undertakes health policy research and analysis in three major areas: national health care expenditures and utilization, hospital costs and utilization, and long-term care. Staff of the intramural research program have been involved in research on the problems of financing long term care for a number of years. In addition, staff are conducting research on health, social, and residential services for physically and mentally impaired elderly.

Long Term Care Studies Program

Using such large data sets as the National Long Term Care Surveys, The National Morality Followback Survey, and the National Nursing Home Survey, the NCHSR's Long Term Care Studies Program undertakes studies on problems such as long-term care expenditures; the feasibility of alternative financing and reimbursement strategies; and the types of care that might be required for particular levels of functional disability. The

following list reflects the FY 1989 publications and conference presentations of the Long Term Care Studies Program:

Authors: Murtaugh, C., L. Cooney, R. DerSimonian, H. Smits, and R. Fetter
Title : Nursing Home Reimbursement and the Allocation of Rehabilitation Resources
Source : Health Services Research, 1988.

Authors: Jackson, M.E., M.L. Drugovich, M.D. Fretwell, W.D. Spector, J. Sternberg, and R.B. Rosenstein
Title : Prevalence and Correlates of Disruptive Behavior in the Nursing Home
Source : Journal of Aging and Health, 1989.

Authors: Spector, W.D. and M.L. Drugovich
Title : Reforming Nursing Home Quality Regulation: Impact on Cited Deficiencies and Nursing Home Outcomes
Source : Medical Care, 1989.

Authors: Spector, W.D., M.C. Kapp, R.T. Tucker, and J. Sternberg
Title : Factors Associated with Presence of Decubitus Ulcers at Admission to Nursing Homes
Source : The Gerontologist, 1989.

Authors: Stone, R.
Title : The Feminization of Poverty and the Elderly
Source : Women's Studies Quarterly.

Authors: Kemper, P.
Title : Case Management Agency Systems of Administering Long Term Care
Source : Gerontological Society of America annual meeting

Authors: Murtaugh, C.
Title : Estimates of the Risk of Nursing Home Use in Later Life
Source : The American Public Health Association annual meeting

Authors: Sternberg, J. and W.D. Spector
Title : The Prevalence of Decubitus Ulcers: Issues of Concern
Source : National Pressure Ulcer Advising Panel Consumers Conference

Authors: Kapp, M.C. and W.D. Spector
Title : Risk of Rehabilitation and Subsequent Death for Elderly Nursing Home Residents
Source : Gerontological Society of America annual meeting

Authors: Spector, W.D., R.B. Rosenstein, W. Freiberger, and M. Kapp
Title : Functional Change and Discharge Status Patterns: New Admission Nursing Home Cohort
Source : Gerontological Society of American annual meeting

Authors: Spector, W.D. and C. Phillips
Title : Staff Turnover as an Indicator of Quality of Care in American and Australian Long-Term Care Facilities
Source : Gerontological Society of America annual meeting

Authors: Kapp, M.C., A.M. Eichorn, and W.D. Spector
Title : Quality of Care in Nursing Homes: Indicators for New York and Texas
Source : American Public Health Association annual meeting

Authors: Murtaugh, C. and R. Stone
Title : The Elderly Population with Chronic Functional Limitations: Implications for Home Care Eligibility
Source : American Public Health Association annual meeting

Authors: Stone, R. and P. Kemper
Title : Spouses and Children of Disabled Elders: Potential and Active Caregivers
Source : Gerontological Society of America annual meeting

Authors: Stone, R.
Title : Spouses and Children of Disabled Elders: Current and Future Patterns of Caregiving
Source : Conference on Caregiving in the 21st Century sponsored by Stanford University and the Veterans Administration conference

Authors: Stone, R.
Title : The Competing Demands of Caregiving and Employment
Source : American Society on Aging

Authors: Stone, R.
Title : Estimating the Size of the Disabled Elderly Population: Implications for Public and Private Long Term Care Insurance
Source : Conference on Long Term Care Insurance sponsored by Health Insurance Association of America, the American Association of Homes for the Aged, and the American Health Care Association

Authors: Stone, R.
Title : National Data on Informal Caregivers: Implications for State Long Term Care Planning
Source : National Association of Health Data Organizations annual meeting

Authors: Stone, R.
Title : Elder Care and Work: Legislative Initiatives
Source : Eastern Region of the Council of State Governments annual conference

Authors: Stone, R.
Title : Informal Caregivers of the Elderly: Barriers to Family Care
Source : Conference on Barriers to Family Caregiving sponsored by Duke University and the Alzheimer's Association

National Medical Expenditure Survey

In FY 1989, work on the 1987 National Medical Expenditure Survey (NMES) continued. This survey will provide a unique data base on how the population uses health care, what they pay for this care, and how we finance these expenditures. A substantial amount of new information on the elderly and long term care is being collected. The national household survey of the civilian noninstitutionalized population includes an oversampling of groups of particular policy interest, including the elderly. In addition to the core data on use, expenditures, health insurance, and sociodemographic variables collected for the noninstitutionalized population, the 1987 NMES household survey has a new focus on long term care. For example, data are being obtained on charges and sources of payment for both formal and informal caregivers and on various measures of health status and functional limitations of the noninstitutionalized long term care population.

The NMES provides a unique opportunity to examine the utilization and expenditures for long term care provided in the community and in institutions. To permit estimates of the utilization and expenditures associated with community based care, the Household Survey Component (HHS) of NMES was designed to include an oversample of elderly and functionally impaired individuals. Approximately 6,000 elderly and 13,000 functionally impaired elderly are included in the data. A parallel survey was conducted among 10,000 residents of nursing homes and homes for the mentally retarded. In both surveys, respondents were followed as they entered and were discharged from institutions.

Data from the Household Component

The NMES HHS questionnaire is designed to collect information concerning all utilization, expenditures, sources of payment for health care and insurance coverage in 1987. In addition to questions concerning use of physician-based services, visits to emergency rooms, outpatient departments, hospitalizations, and expenditures related to prescribed medicines and other medical expenses, data are collected on the use of and charges for home health services, including care provided by a medical person, a friend, relative, homemaker or home health aid.

Basic demographic information is collected for all respondents (e.g., race, gender, education). Of special importance for elderly health financing issues are questions of assets. Detailed income information (paralleling CPS income questions) as well as home ownership questions were asked. Data concerning house modifications related to functional impairments and the relationship between onset of functional limitations and selling a home were included in the study.

Functional ability and use of community-based care is measured at two points in time, during the first and fourth round of interviewing. The questions include the Activities of Daily Living and Instrumental Activities of Daily Living developed by Katz. Both measures of difficulty and the need for personal assistance of the use of special equipment are included in the instrument. Utilization of community-based care, such as senior centers, adult day care centers, enrollment in programs such as "meals on wheels," and use of special transportation designed for the elderly or handicapped are measured. Data are also available concerning supplemental income provided by friends or relatives not living in the household.

The data also include several questions concerning the effects of providing care to an elderly or functionally impaired person. These questions include the effects on employment (e.g., working fewer hours due to providing care, taking time off, the need to quit a job, the effect on income) as well as measures of stress related to such care (e.g., amount of free time, strain on income, effects on sleep). For those providing care to someone outside the household, additional items measure the types of care provided and amount of time spent delivering that care.

Condition information associated with disabilities and utilization are collected. In addition, measures of prevalence for several chronic conditions such as hypertension, arthritis, diabetes, emphysema, and heart disease are possible, regardless of whether the condition was related to utilization during 1987. Prevalence measures are also possible for developmental disabilities such as epilepsy, cerebral palsy, autism, and mental retardation.

Several of the data elements address the question of access to care. These questions include whether the person has ever or is currently on a waiting list for a nursing home and whether the person did not receive care for some reason when he or she needed it.

Institutional Population Component

Two institutional groups are included in the Institutional Population Component (IPC) of NMES: those individuals in nursing homes and those individuals in homes for the mentally retarded. The design of the IPC samples individuals at both the beginning of 1987 ("Current Residents") as well as throughout 1987 ("New Admissions"). This provides a sample base that includes both long-term residents as well as short-term residents and permits analyses concerning living arrangements and use of community-based care prior to institutionalization. Data have been collected on approximately 6,000 nursing home residents (3,350 current residents; 2,570 new admissions) and 4,500 residents of homes for the mentally retarded (360) current residents; 862 new admissions). Interviews were conducted both with an appropriate respondent from the institution and, whenever possible, with a relative or guardian of the resident ("Next of Kin"). The next of kin reported on the health status of the resident prior to admission and use of community-based services.

The Baseline questionnaire, collected once per resident, obtains information on the resident's demographic characteristics, history of admissions to institutions and living arrangements prior to the present admission, current functional ability (the same ADL/IADL measures used in the HHS), the need for personal assistance or the use of special equipment related to the functional limitation, primary diagnosis upon admission, employment status prior to admission, and measures of prevalence for both developmental disabilities and chronic conditions similar to those asked of HHS respondents. All of the questions concerning health status (e.g., ADL measures) are recollected in the End of Year Questionnaire.

The Institutional Use and Expenditure Questionnaire is administered every four months. Information on all ambulatory care that residents receive both inside and outside the facility and for each general or short-term hospitalization are collected. Expenditure information, including source of payment and types of services included in the charge, is collected for charges associated with the institutionalization.

Detailed information concerning the resident's living arrangements, functional ability, use of special equipment, and income prior to institutionalization are provided by the next of kin. This questionnaire includes a set of questions with respect to providers of care in the home that parallel the HHS component (e.g., household residents who helped the resident with bathing or dressing).

The next of kin is also asked to report on the use of community-based services by the respondent. Utilization of health care services (e.g., physician's, emergency rooms, outpatient departments, etc.), prescribed medicines, and other medical equipment is collected as well as the associated total charges (per quarter) and the sources of payment.

The following bibliography reflects aging-related and minority papers/publications completed by staff of the National Medical Expenditure Study in FY 1989:

Authors: Leon, Joel and Lair, Tamra
Title : The 1987 National Estimates of the Functionally Limited Elderly
Source : National Medical Expenditure Survey Research Findings 4

Authors: Lair, Tamra and Lefkowitz, Doris
Title : Characteristics of Nursing Home Residents: Findings from the 1987 NMES
Source : Annual Meeting of the Gerontology Society of America

Authors: Lair, Tamra et al.
Title : Mental Illness and Impact of Nursing Home Reform
Source : Annual Meeting of the Gerontology Society of America

Authors: Freiman, Marc et al.
Title : Nursing Home Reform and the Mentally Ill
Source : Annual Meeting of the American Public Health Association

Authors: Stone, Robyn and Short, Pamela Farley
Title : Effects of Care Giving for Disabled Elders
Source : Annual Meeting of the American Public Health Association

Authors: Leon, Joel and Short, Pamela Farley
Title : Use of Home and Community Services by Elderly Persons with Functional Disabilities
Source : National Medical Expenditure Survey Research Findings 5

Authors: Leon, Joel
Title : Availability of Special Nursing Home Programs for Alzheimer's Disease Patients
Source : Annual Meeting of the Gerontology Society of America

Authors: Short, Pamela Farley, Cornelius, L.J., and Goldstone, D.E.
Title : Minority Uninsured in the United States
Source : Conference for Health Care to the Poor and Underserved

Authors: Cornelius, L.J.
Title : Access to Care for Black, White and Hispanic Children: A 1987 Profile
Source : Annual Meeting of the American Public Health Association

Authors: Beauregard, Karen, Cunningham, Peter and Cornelius, L.J.
Title : Access to Health Care Among Native Americans
Source : Annual Meeting of the American Public Health Association

HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Health Professions

Aging

Four prototype regional Geriatric Education Centers (GECs) originated in 1983. In 1985, 16 additional centers were established, and in 1986 the number of centers reached a total of 22. In FY 1987 a total of $9,306,742 was awarded for geriatric activities. Included in this amount was $8,570,154 to support 31 GECs. These centers involved over 200 professional schools, teaching hospitals, teaching nursing homes, and other entities located in 25 states and Puerto Rico. In FY 1988, $9,543,122 supported 33 GECs. In FY 1989, $10,653,123 supported 38 GECs. These centers emphasize training of health professions faculty so that they will be more knowledgeable regarding the special health problems of geriatric patients in order to properly educate and train health professions students in this area. Multidisciplinary curriculum development, expert consultation, resource sharing, technical assistance, and training for health practitioners are also carried out within the geographic areas served by these centers. The ultimate goal is to improve the quality of health care delivered by health professionals so that the independence and mobility of the elderly may be increased. In June 1989, the leaders of the nationwide network of Geriatric Centers participated in a workshop in Milwaukee, Wisconsin to explore new emphases such as health promotion, minority aging, rural elderly, and chronic diseases. A contract in the amount of $74,148 was awarded in FY 1988 to Marquette University for this fifth GEC workshop.

Twenty-one Nursing Special Projects were supported and awarded $2,412,811 in FY 1989. These projects included inservice educational programs for licensed practical nurses working with the aged, gerontological training programs for nurse educators, and educational programs for practicing nurses in the assessment and management of the frail elderly. Project activity was based in acute care settings and in the community as well as nursing homes.

In FY 1989, $1,460,069 was awarded to 13 nurse practitioner programs to prepare registered nurses as geriatric/gerontological nurse practitioners. As nurses with advanced academic preparation and clinical training, they are prepared as primary health care providers to manage the health problems of the elderly in a variety of settings, such as long term care facilities, ambulatory clinics and the home. They provide nursing care which includes the promotion and maintenance of health, prevention of disease, assessment of health needs, and long term nursing management of chronic health problems. Emphasis is placed on teaching and counseling the elderly to actively participate in their own care and to maintain optimum health.

The Advanced Nursing Education Program awarded $1,554,004 to 10 programs to support curricula development to prepare clinical specialists in the care of the aged. Graduates of these programs are prepared broadly to meet a wide range of needs relative to the elderly in many settings, but are particularly prepared to deal with the older individual who is acutely ill. In addition, the program prepares nurses who can teach and do research in this important field.

The Area Health Education Center (AHEC) program awarded a total of $661,305 to the 13 AHECs which indicated emphasis in geriatric education. These educational and training activities benefitted an estimated population of 298,164 (including trainees). Five of the awards were for special initiatives which included developing geriatric personnel certification programs and training in health promotion/disease prevention in older individuals.

All 37 Physician Assistant Training program grantees have instituted training activities in geriatrics. Funds in the amount of $106,291 were awarded among 11 of the grantees specifically for their efforts in this area. An estimated 1,774 trainees would be affected.

In FY 1989, twenty-seven predoctoral grantees and 113 graduate program grantees under the Family Medicine Training program indicated they were actively involved in the development, implementation and evaluation of their geriatrics curriculum and training. Twenty-three of the residency program grantees received funds totaling $1,481,819 specifically for developing and enhancing geriatrics curriculum and training. These awards ranged between $13,150 and $135,090, the largest going to the University of Connecticut for expansion of the training in geriatric medicine. In addition, 33 faculty development programs reported that they provided geriatrics training. Eight Family Medicine Departments Program grantees have established a geriatrics component and $403,025 was awarded specifically for this purpose.

The General Internal Medicine and General Pediatrics Residency Training programs reported 30 grantees who provided geriatric medicine training to approximately 186 residents. A total of $136,140 was awarded to 5 of the programs for their efforts. In addition to graduate training, 2 grantees under the faculty development program indicated that their geriatric emphasis would affect about 38 faculty, but no specific funds were received for these activities.

One Preventive Medicine Residency Training grantee indicated that they are including a geriatric curriculum in the program, from which 12 residents will benefit.

Nine grantees receiving support for Podiatric Primary Care Residency Training under the new section 788(e) authority have included curricular emphasis in geriatric health which will benefit an estimated 72 residents. These grantees received a total of $145,650 for this purpose.

Under the program for Faculty Training Projects in Geriatric Medicine and Dentistry (section 789(b)), 23 grantees received a total of $3,100,000 to provide geriatric faculty training experiences for 38 physician participants and 26 dental participants.

National Institute on Alcohol Abuse and Alcoholism

AGING

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) supports research on the incidence and prevalence of alcoholism and alcohol abuse among the elderly and on the causes and consequences of problem drinking among this age group.

NIAAA funds aging-related research through its extramural research program and through collaborative activities with other Federal agencies. One of the 12 national alcohol research centers supported by the Institute focuses on aging and alcohol. In its second year of funding, overall goals of this center are (1) to develop strategies for early diagnosis and treatment of alcoholism in older individuals, and (2) to determine how alcohol interacts with the normal aging processes to produce central nervous system abnormalities. The multidisciplinary research takes advantage of state-of-the-art non-invasive technologies such as PET scanning and magnetic resonance imaging to investigate alcohol-related abnormalities of the central nervous system.

Efforts in basic research are exploring the role of aging in the outcome of excessive alcohol consumption. Current studies range from assessments of anatomical, physiological, biochemical and behavioral changes after chronic alcohol use to determinations of how alcohol use confounds problems associated with aging. For example, does alcohol use in the elderly worsen certain disease states, such as osteoporosis, cardiovascular problems, cancer of the breast and cervix in menopausal women, and diabetes and peripheral neuropathy? The current hypothesis is that chronic alcohol consumption accelerates the aging process. In other words, problems normally associated with old age could become a problem in younger individuals who drink excessively. Research is being conducted to determine the validity of this hypothesis especially in the actions of nerve cells in the brain. Also, diagnostic profiles are being developed to assess brain dysfunction as it relates to emotional and motivational changes in alcoholics. The research supported by NIAAA will provide valuable clues in ascertaining the magnitude of alcohol problems in the elderly and in formulating strategies to reduce their impact.

Other research is investigating the role of life stressors and coping resources in excessive drinking among late middle age and older adults. This line of research will help identify why some people develop or resume problem drinking when faced with stressful life situations while others do not. It will also help identify the social and situational factors that promote or inhibit problem drinking. Still other projects are examining the question of whether special programs (i.e., treatment or prevention services) are needed for older problem drinkers.

National Institute of Mental Health

MENTAL DISORDERS OF THE AGING RESEARCH

Introduction

Between 1900 and 1984, the percentage of elderly in the total U.S. population rose from 4 percent to 12 percent. By the year 2030, it is projected that there will be more than 64 million persons over 65 and more than 30 million over 75. As the population ages, the mental health problems of the elderly gain prominence as a major public health concern.

The dementias, including Alzheimer's disease, represent a devastating problem in the elderly population and will become more prevalent as the U.S. population ages. At present, almost 3 million people 65-and-older, mostly women, suffer from a dementia (because of the special interest in Alzheimer's Disease (AD), it is included as a separate section at the end of this report). In addition, depression is a relatively frequent and often unrecognized problem among the elderly, contributing to the high suicide rate within this population. In fact, white males over age 85 have the highest recorded suicide rate of any group in the population (55.8/100,000).

Mental illness is frequently found among the institutionalized elderly. Five percent of the Nation's aged live in institutions. Of these, about 12 percent are in mental hospitals, with the remainder in nursing and other types of homes for the aged and chronically ill. Geriatric patients occupy 20 percent of beds in public psychiatric hospitals, and an estimated 80 percent of those age 65 and older in nursing homes have some degree of mental impairment.

Because the number of elderly persons is increasing rapidly and mental problems are common in this age group, NIMH has identified disorders of the aging as among the most serious mental health problems facing this Nation and is currently involved in a number of activities relevant to aging and mental health. Highlights of this work are described below.

Depression in the Elderly

Depressive illness is now widely recognized as a major cause of morbidity and mortality in old age. Although it represents a significant public health concern by virtue of its high cost in human suffering, disability and potential for suicide, until recently, systematic information and specific criteria for optimal treatment have been unavailable. Some important new findings have emerged this year.

Investigators in geriatric depression have been isolating factors which differentiate late-life onset depression from that more

commonly seen in younger adults. The researchers have found that geriatric depression is more commonly characterized by delusions and by cognitive impairment and that it has a poorer prognosis in terms of relapse and recurrence.

Several sleep parameters are also commonly affected in geriatric depression and can help to differentiate it from other disorders: 1) reduced amount of rapid eye movement (REM) time in sleep prior to treatment is strongly associated with recurrence of depression; 2) response to one night of total sleep deprivation correctly differentiates patients with depressive pseudodementia from patients with Alzheimer's disease or other dementias; and 3) lengthened REM latency is a significant predictor of mortality in patients with mixed depression and cognitive impairment.

Research has focused also on medications used to treat geriatric depression. Tricyclic antidepressants (TCAs), such as imipramine, are widely used and show good results in a large proportion of adults with depressive disorder. However, elderly patients are particularly sensitive to the side effects of TCAs, and there is some evidence that the percentage of elderly depressed patients showing a complete therapeutic response to TCAs is lower than in other depressed patients. Investigators have shown that the inhibition of serotonin uptake into platelets by imipramine was markedly reduced in elderly depressed patients compared to younger patients and young and older normal controls. This reduced sensitivity to imipramine may explain the reduced responsiveness of geriatric patients to it and other TCAs.

Late Life Onset Schizophrenia

In a pioneering study of schizophrenia which manifests itself for the first time after the age of 45, investigators have postulated that this atypical disorder is actually a heterogeneous entity with different subtypes, some of which may be identifiable with specified clinical, neuropsychological, and brain morphological evaluations (including magnetic resonance imaging) and which may be associated with differences in neuroleptic response. Preliminary findings suggest that these patients may have larger ventricles than age-matched normal controls.

Anxiety in the Elderly

Research has shown that nearly 40 percent of geriatric patients with major depression also meet criteria for anxiety. Additionally, anxiety is a common feature of many medical conditions (e.g., gastrointestinal, cardiovascular, and pulmonary disease) in the elderly and is a side effect of many commonly used medications. Unfortunately, antianxiety agents have been found to have particularly strong cognitive and behavioral side effects, especially in those older persons whose cognitive functioning is compromised due to a mild or moderate dementia such as that seen

in early-stage Alzheimer's disease.

Geriatric Psychopharmacology

Studies continue to evaluate the effects of age, gender and additional relevant variables on the actions, effects, and movement through the body of psychotropic drugs. Across a large number of studies, investigators have found that various widely used benzodiazepines with approximately equivalent tranquilizing properties clinically have differing effects in terms of sedation, and impairments of memory and performance. The differing effects of the drugs are explained in part by variations in the ways the drugs interact with tissues. However, they are also mediated by the differential receptor binding of these agents. Although, for many benzodiazepines (clonazepam, estazolam, lorazepam, triazolam), receptor binding is related to brain concentrations of the drugs according to an s-shaped function, alprazolam appears to interact with benzodiazepine receptors in a unique way. Furthermore, receptor binding is influenced by various other factors, including stress and aging. Current studies are emphasizing the effects of chronic (i.e., long-term) use of benzodiazepines and of alcohol, as well as changes with age.

In other developments, investigators have found that normal elimination from the body of chlordiazepoxide, a tranquilizer, is reduced (and its half-life prolonged) in elderly men but not in elderly women--a pattern that has been noted with various other benzodiazepines. Research also has demonstrated that the sleep disorder (rebound insomnia) that often occurs following discontinuation of triazolam, another tranquilizer can be lessened by decreasing dosage over a period of time until the patient is weaned from the drug.

Memory, the Brain, and Aging

As humans age, their ability to learn and remember may deteriorate. It is not clear why this happens or how it can be prevented or treated. Dr. Michella Gallagher, University of North Carolina, has developed a useful animal model for this human impairment. The model uses the natural swimming ability of rats which requires them to locate a platform under cloudy water using past experience (memory) as a guide. This test permits the study of both spatial memory (memory of spatial relationships and the actual pattern of the physical arrangement of objects) and motor memory (memory of physical actions necessary to perform a task). Dr. Gallagher has reported that the memory problem for aged rats was specifically notable in spatial memory, not in motor memory. This result means that the specific neurobiological mechanisms for memory loss due to old age can be explored and raises the hope for specific therapies and prevention.

Evidence from patients with Alzheimer's disease suggests that the

basal forebrain cholinergic system, which produces the neurotransmitter acetylcholine, plays an important role in memory. Scientists in the NIMH Intramural Laboratory of Neuropsychology have found that recognition memory in normal monkeys can be improved by administration of the cholinesterase-inhibitor physostigmine and impaired by the cholinergic muscarinic-receptor blocker scopolamine. Spatial memory has also been found to be impaired by scopolamine. THC (the active ingredient in marijuana) and scopolamine (an anticholinergic agent) impair memory after different lengths of delay, suggesting that THC acts on memory through a noncholinergic mechanism.

A number of diseases as well as the normal aging process cause the slow death of neurons in the brain. Recently scientists have recognized that a number of chemicals - neurotrophic factors - can influence the health and growth of neurons. Dr. Forrest Haun of the Medical College of Pennsylvania is testing a variety of these factors in brain-injured animals to determine if any of these factors might reduce cell death and possibly restore behavioral function. He has recently found a novel factor that is effective in reducing cell death of damaged cortical neurons and, in behavioral tasks that reflect cortical function, the treated brain damaged animals show improvements over controls. Dr. Haun is in the process of chemically identifying this neurotrophic factor which is biochemically distinct from all previously known growth factors.

Ten years ago, scientists in an NIMH laboratory developed methods that formed the foundation for the new field of imaging of local physiological processes, biochemical processes, and local functional activities in the nervous system. The most recent technique developed by NIMH researchers is designed to measure regional rates of protein synthesis in brain.

Protein synthesis is probably the most important biochemical process underlying the development, maturation, plasticity, maintenance and long-term regulation of the nature and degree of functional activity of the nervous system. The structural, functional, and metabolic properties of tissues largely reflect the role of structural and enzymatic proteins. In the nervous system proteins serve as hormones and are the parent compounds of peptide neurotransmitters. It is, therefore, certain that changes in protein synthesis can and do alter function and that some mental and neurological dysfunctions reflect disturbances in this vital biochemical process. The technique to measure rates of protein synthesis has already proved useful in studies of neural regeneration, plasticity, and the involutional changes which may occur in the process of aging.

In keeping with the NIMH research priority on Alzheimer's disease and other mental disorders of the elderly, researchers at the University of California, San Diego are examining how normal aging and aging-like behaviors are related to structural changes in the hippocampus. Magnetic resonance images (MRI) of hippocampal

regions of normal men and those with amnesia indicate that important structural changes accompany the memory loss that defines amnesic patients.

Researchers at the Salk Institute and at the University of California, San Diego, recently made this finding by using a high resolution technique for the non-invasive imaging of the human hippocampus. This new technique permits them to view the hippocampus in exquisite detail, revealing for the first time brain abnormalities in patients with amnesia. It has shown that, in memory-impaired patients, the hippocampus is abnormally small -- almost half the size seen in normal controls. Additionally, the size of some nearby brain structures was also abnormal. These results clearly illustrate the value of anatomical studies and state-of-the art imaging approaches in understanding the sources of severe cognitive deficits.

As the information provided above indicates, many of the Nation's elderly suffer from mental disorders and many researchers are working to understand, treat, and prevent these problems. Much work is also being done on various aspects of Alzheimer's disease. In depth discussion of the work completed on Alzheimer's may be found in the FY 1991 Moyer Report on Alzheimer's Disease.

NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

AGING

INTRODUCTION

Aging research is entering an era of unprecedented challenges and opportunities. Because no single process explains the multiple and interacting changes that occur with age, the Federal government, through the National Institute on Aging (NIA), implements a dynamic research program that identifies promising clues to many of the biomedical, social, and behavioral changes associated with age. Simultaneously, the Institute supports applied research efforts on potential interventions to ameliorate the consequences of such common problems as falls and urinary incontinence. Of equal importance the Institute plays a leading role in aging research through its support of training and career development.

One of the Institute's highest priorities is studying Alzheimer's disease. This year much exciting progress has been made, including an advance toward a diagnostic test. In addition, new findings on how and why brain cells die as the disease progresses may eventually show us a way to halt or reverse this disease. (See the separate report on Alzheimer's disease for specific research highlights.) Institute priorities also include investigating the basic mechanisms of aging, reducing fractures in frail older people, researching health and effective functioning in old age, improving long term care, fostering an increased understanding of aging needs for special populations, and improving career development training opportunities in geriatrics and aging research.

Other NIH institutes that also support research on aging or aging-related concerns are the National Cancer Institute (NCI); the National Heart, Lung, and Blood Institute (NHLBI); the National Institute of Dental Research (NIDR); the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); the National Institute on Neurological Disorders and Stroke (NINDS); the National Institute of Allergy and Infectious Diseases (NIAID); the National Eye Institute (NEI); the National Institute of Environmental Health Sciences (NIEHS); the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS); the National Institute on Deafness and Other Communication Disorders (NIDCD); the Division of Research Resources (DRR); the National Center for Nursing Research (NCNR); and the Office of the Director (OD).

Older Patients Often Experience Discriminatory Health Care Practices

It is increasingly acknowledged that lifestyle changes at any age can improve a person's quality of life. Yet, in a study conducted by NIA grantees Dr. Rosalie F. Young at Wayne State University in Detroit, Michigan, and Dr. Eva Kahana at Case Western Reserve University in Cleveland, Ohio the overwhelming conclusion is that older patients often are denied access to information and recommendations that would lessen their risk of future illness. Further, this problem occurs because physicians generally are not trained to communicate effectively with older people and may lack the knowledge that preventive measures are beneficial for even the oldest people.

Dr. Young and her colleagues questioned 246 cardiac patients following their discharge from several Detroit hospitals. All respondents spoke English and had no evidence of severe cognitive impairment. Questions concerned personal health, use of health care facilities, general well-being, and knowledge of heart disease and ways to reduce the risk of future cardiac problems. The investigators found major differences in the information and instructions given to patients age 60 and above compared with that given to younger patients.

The study found that people in the older age group reported receiving less information and instruction than people in the younger age group. With respect to physician-generated information, 38 percent of the older group received no information about heart attacks compared with 21 percent of the younger group. Older people were told less information than younger people about weight, diet, exercise, reduction or cessation of smoking, reduction of stress, and enrollment in rehabilitation programs. For example, nearly half of the younger group were told to stop smoking, while only about one-quarter of the older group were given the same guidance.

Cardiac rehabilitation programs are extremely beneficial to recuperating heart patients at any age, regardless of the extent of the patients' disease or their general health. Yet, investigators found that only 28 percent of the older age group were advised by their physician to participate in such a program, compared with 52 percent of the younger group.

Another example of how older people are generally less apt to receive state-of-the-art health care than younger people is found in the work of NIA grantee Dr. Jeanie Kayser-Jones at the University of California, San Francisco who correlated the professional and personal environments in nursing homes to the quality of care the patients received.

In in-depth interviews of 100 physicians between the ages of 29 and 79, Dr. Kayser-Jones found that 53 percent do not believe that older patients should receive maximum evaluation and

treatment for acute illnesses. As a result, patients over 80 years of age often receive less aggressive care than their younger counterparts.

Dr. Kayser-Jones studied how physicians make treatment decisions for their older nursing home patients with acute illnesses. She found that several factors act as deterrents to aggressive treatment. These factors include a fear of malpractice suits should treatment fail, a distrust of reports from nursing home staffs, and an uncertainty as to Medicare reimbursement. Dr. Kayser-Jones also found that 48 percent of older nursing home residents were transferred to hospitals not for clinical reasons, but because nursing homes were poorly staffed with inadequately trained nurses, nurse-physician communication was ineffective, and families wanted better care for relatives than the nursing homes provided.

Investigators encountered other problems in nursing homes. Nurses often diagnosed a patient's complaint to the physician by phone, a practice that relies heavily on the verbal and assessment skills of the person filing the report. Many nursing homes were ill equipped to handle severe illness, and staff, therefore, routinely urged physicians to transfer patients to acute care hospitals. Physicians reported reluctance to perform tests that might require followup treatment.

The authors point out that while many nursing homes are of high quality, problems in others must be addressed. Dr. Kayser-Jones suggests encouraging rapid and skillful health assessment of patients, monitoring their subtle changes, following through on diagnostic tests, formulating comprehensive treatment plans, evaluating results after treatment, and coordinating nursing home staff and shifts.

In a third example of age discrimination, NIA grantees Drs. Gaylene Becker and Sharon Kaufman at the University of California, San Francisco examined data from various studies related to the availability of rehabilitation therapy for older patients and initiated their own research on stroke rehabilitation. They conclude that though rehabilitation is beneficial for many older persons, it is not routinely offered. The decision to introduce rehabilitation therapy after a stroke depends upon the patient's recovery potential, yet chronological age is generally assumed--without scientific base--to affect recovery.

Of all illnesses occurring later in life, stroke is the most physically debilitating. Stroke patients comprise the largest single group of older patients in physical rehabilitation settings. Investigators found that rehabilitation facilities, however, are very selective when admitting patients over age 80. Only those who demonstrate the greatest potential for progress are selected so that therapists can be assured of at least some success. As a result, persons chosen for

rehabilitation are most often under 80 years of age, thus perpetuating faulty perceptions regarding age.

Drs. Kaufman and Becker found that older stroke patients who have multiple illnesses or cognitive impairment generally are not aware of the purpose of their therapy. A stroke patient's attention may focus on physical losses rather than on ways to overcome them. In response, health care professionals may develop a sense of futility about therapy for older persons. The investigators speculate that the potential conflict between patient goals and professional goals may significantly reduce access to rehabilitation.

These studies demonstrate that negative values about old age infiltrate health care choices, even among health care professionals.

Falls of Older People Have Many Causes

Falling is a major cause of disability among older people. Each year, falls occur in approximately one-third of all persons age 65 and older who live at home. About 50 percent of those who fall do so repeatedly. A common accident among older Americans, falls cause more than 200,000 hip fractures annually. They are also the leading cause of accidental death in men and women over 85.

Research supported by the NIA focuses on determining the extent to which physical frailty and risk of injury can be reduced in older people. To learn which older individuals were at greatest risk of falling, NIA grantee Dr. Mary Tinetti at the Yale University School of Medicine in New Haven, Connecticut studied more than 300 people 75 years of age and older who were living in the community.

At the beginning of Dr. Tinetti's study, the participants underwent a thorough evaluation, including standardized measures of their physical and mental health, strength, reflexes, balance, and gait. Participants recorded their falls in a diary and were called every other month to discuss the number of falls and the circumstances surrounding their occurrence.

During the year the study was conducted, 32 percent of the participants fell at least once. Of those who fell, 24 percent were seriously injured, including 6 percent who suffered fractures. Twenty-six percent of those who fell reported that they had curtailed shopping, housecleaning, or other activities for fear of falling.

Although some falls have a single, obvious cause, Dr. Tinetti found that most are due to a combination of risk factors. She observed that use of sedatives, changes in mental status, lower extremity disability, foot problems, and balance and gait abnormalities were significant risks for falling. Other

risk factors included changes in vision, hearing, muscle strength, and reflexes. In addition, hazardous conditions such as poorly secured rugs, cluttered walkways, or loosely fastened handrails contributed to the risk of falling.

Dr. Tinetti also discovered that the tendency to fall increased with the actual number of risk factors present, from 8 percent for individuals with no risks to 78 percent for those with 4 or more risk factors. Her research suggests that it may be possible to prevent falls by modifying even a few of these risk factors.

Dr. Tinetti and others have found that most older people fall during their usual daily activities, such as walking or changing position (for example, rising from a sitting to a standing position). A minority of falls--about 5 percent--occur during clearly hazardous activities, such as climbing on chairs or ladders or participating in sports. About 10 percent of falls occur on stairs, with descent more hazardous than ascent.

Even those falls that do not result in injury may have serious psychological consequences. An older person who has fallen once tends to reduce his or her activity because of a fear of falling again. In addition, in an effort to prevent falls, family members and health care providers may discourage physical activity. This decrease in physical activity is particularly hazardous because inactivity itself leads to an increase risk of falling. Falls and frailty are mentioned as a contributing factor in about 40 percent of nursing home admissions.

Now that researchers have identified the factors that increase the risk of falling, falls can no longer be considered random, unpredictable events. The first step in preventing falls is identifying the disabilities and other risk factors that predispose older people to fall. Studies are underway to identify interventions that will minimize the risk of falling without compromising an older person's independence.

Risk of Heart Disease May Be Greater for Hostile Individuals

Individuals who are hostile, especially if they are arrogant, argumentative, surly, and rude, appear to increase their chance of having coronary heart disease (CHD). That's the finding of researchers at the University of Maryland at Baltimore County (UMBC) and NIA's Gerontology Research Center (GRC) in Baltimore, Maryland.

It has long been suspected, but not fully confirmed, that individuals displaying type A personality characteristics such as hostility, competitiveness, impatience, and a heightened sense of time urgency, are more likely to develop cardiac disease. One research project, the Western Collaborative Group Study, showed that type A behavior doubled the CHD risk. However, another study, the Multiple Risk Factor Intervention Trials (MRFIT),

showed little or no association between type A traits and death from heart disease or nonfatal heart attacks.

Dr. Theodore Dembroski at the UMBC, NIA intramural scientist Dr. Paul T. Costa, and their colleagues looked at one personality trait commonly found in type A people--"potential for hostility." They examined the relationship between hostile behavior and an increased risk for coronary death and nonfatal heart attacks among nearly 600 participants in the MRFIT. The participants ranged in age from 35 to 75 years old.

The investigators measured three interrelated components of hostility, as well as overall type A behavior, as possible predictors of sudden death and nonfatal heart attack. After adjusting for known coronary risk factors such as high blood cholesterol, smoking, and hypertension, they found that "potential for hostility" was positively linked to an increased risk for heart disease, especially in younger participants. In and of itself, however, type A behavior was not found to be an independent risk factor for CHD.

These findings suggest that hostility may be unhealthy enough to jeopardize one's health. Future health risk profiles may be devised with this behavior trait in mind.

Depression Can Cause Debilitating Effects

Depression can be defined in two ways. The first is a medical orientation that refers to a prolonged psychiatric disorder. The second is a lay term which encompasses a general feeling of sadness.

A new study finds that both types of depression can be as debilitating as a serious heart condition. In fact, it is more disabling than most chronic physical conditions. People with traditional symptoms of depression report more days in bed and perceive more physical pain than patients experiencing back, lung, or gastrointestinal problems, angina, or diabetes. Of these conditions, only serious heart conditions can cause more days in bed and only arthritis can be more painful.

These findings come from the Medical Outcomes Study (MOS), supported in part by NIA, and conducted by the Rand Corporation of Santa Monica, California. The MOS is the largest and most comprehensive patient-oriented observational study to compare medical, psychological, and social outcomes of patients treated at various health care facilities. Investigators included Dr. John Ware at the New England Medical Center in Boston, Massachusetts, Dr. Kenneth Wells at the University of California at Los Angeles' Neuropsychiatric Institute and Hospital and Dr. Alvin Tarlov at the Henry J. Kaiser Family Foundation, Menlo Park, California.

In the MOS, investigators surveyed 22,462 patients and 523 physicians at HMOs, large group practices, and individual practices in Boston, Chicago, and Los Angeles. Participants ranged in age from 18 to 103 years old. The study focused, not on illness per se, but on how the patient actually functions and feels. A cross-section of the total sample participated in tests evaluating physical and social functioning, mental health, health perceptions, and bodily pain.

A key finding from this study is that depression is as disabling as chronic medical conditions in performing routine, daily activities such as walking, dressing, and visiting friends. Moreover, depression in combination with a chronic medical condition greatly compounds the dysfunction that may be associated with the medical problem alone. Performance of everyday activities is particularly difficult for patients suffering both depression and a chronic medical condition. For example, patients suffering from depression and coronary artery disease were twice as likely to have problems with social relationships as patients with only one of these conditions.

In addition, the MOS uncovered significant findings about the effects of physical illnesses. The study found that most chronic conditions make it difficult for a person to conduct everyday activities and maintain a positive attitude. Health perceptions were most negative for patients with congestive heart failure or gastrointestinal disorders and most positive for those with hypertension or back problems. Daily functioning was easiest for people with hypertension and most difficult for those with heart diseases.

In summary, this study demonstrates that depression can cause disability as severe as other major chronic conditions. Further, a patient's physical symptoms may mask the depression. It is essential for physicians to be aware of the influence depression can have on the course of an illness, to make accurate diagnoses, and offer proper care for people who complain even when the complaints are non-specific. According to the investigators, the method they have used to evaluate illness might prove valuable in assessing the overall progress of ongoing treatment because it considers the patient's concerns and monitors for more than one condition.

Further analysis of data will include age-specific differences in the sample population.

Investigators Examine Active Life Expectancy

The U.S. Bureau of the Census estimates that by the year 2000 there will be 4.9 million people in this country who will be at least 85 years of age, a number which will increase to as many as 5.6 million in the year 2060. This projection is based on present population figures as well as on conservative assumptions about declining mortality rates for very old people. However, a

growing body of scientists feel that this prediction could be vastly understated and that the number of people in this age group may actually become more than 200 percent higher than the Census Bureau's highest projections--over 15 million.

One such scientist is NIA grantee Dr. Kenneth G. Manton at Duke University in Durham, North Carolina. Dr. Manton developed a computer model that simulates the effects on longevity of certain behavioral changes. For example, a man at age 30 could conceivably add 15 years to his life by eliminating risks such as smoking and high blood pressure. Therefore, Dr. Manton concludes that many more people could live to join the oldest old age group (those 85 years of age and older) than estimated in conventional projections.

Given the rapidly growing number of very old people in the United States, NIA scientists are investigating the quality of those lives. Will people be active and autonomous, or dependent and in need of care? Dr. Manton used the special assumptions built into his computer model to forecast the number of years very old people can reasonably expect to live without disabling conditions (active life expectancy). His analysis shows that, though life expectancy for men at age 85 is 5.15 years, only 2.63 of those years will be active. For women in this age group active life expectancy is 2.3 of their remaining 6.44 years. Dr. Manton projects that older women will spend more of their remaining days receiving institutionalized care than will men--1.88 years for women as opposed to .9 years for men.

This study also also assessed the influence of chronic conditions on active life expectancy. Dr. Manton estimated that the elimination of dementia, for example, would increase active life expectancy among this age group by 11.4 percent for men and by 26.1 percent for women. He demonstrated that smoking cessation and control of high blood pressure could reduce an individual's future disability.

Dr. Manton observes that ignoring the likelihood of a much larger population of the oldest-old is unwise. He suggests that possibly the only practical response is to maximize the health and functioning of the oldest-old by motivating changes in unhealthy habits.

In another analysis of independent versus dependent aging, NIA grantees Drs. Andrei Rogers and Richard Rogers at the University of Colorado at Boulder and their colleagues linked life expectancy of the oldest old with level of independence.

Four activities of daily living were used to classify an individual's ability to function independently: the ability to eat, bathe and dress oneself, and the ability to move from bed to chair unassisted. The researchers used Katz and coworkers' data from Waves One and Two of the Massachusetts Health Care Panel Study to estimate active life expectancy. Wave One consisted of

interviews with over 1,600 non-institutionalized people age 65 or older. Wave Two consisted of interviews with 1,500 people, some of whom were institutionalized (approximately 89 percent of them from the original Wave One group).

The investigators found a dramatic correlation between age and active life expectancy. For example, at 65 people could expect about 14.7 years of active life expectancy, at 80 people could expect less than half that or 5.6 years, and those people who were 85 could expect about 3.8 years of active life expectancy. Stated another way, the percentage of remaining years that could be lived independently dropped from about 90 percent for age 65 to 67 percent for those 85 years of age. People at any age who were independent could expect to live a majority of their remaining years independently.

The study also looked at active life expectancy for 65-year-old people who were dependent on others at the initiation of the study. The researchers concluded that even these individuals could expect to live 72 percent of their remaining 15.5 years independently. This conclusion was based on the probability of some individuals recovering from whatever condition caused their initial dependency. However, as the population ages, the estimated percentage of years spent independent of others does decrease.

These studies document the increasingly large number of people who can live to celebrate an active 85th birthday. This information can help health care professionals and policy makers plan for the challenges of providing quality care for people in their last years life.

Smoking and Body Fat Studied

GRC researchers have discovered yet another reason to quit smoking. Results of a large-scale study show that cigarette smoking produces a redistribution of body fat which is associated with coronary heart disease. Smokers who quit often gain weight around the hips, a relatively benign region in terms of health effects. This link between smoking and body fat proved true for the younger and older participants.

Hundreds of studies worldwide provide convincing evidence of the harmful effects of cigarette smoking, which takes a major toll on the heart, lungs, blood vessels, and other organ systems. According to the U.S. Surgeon General's Office, male cigarette smokers are at 22 times the risk for lung cancer and more than one of every six deaths in the nation can be traced to cigarettes.

Although about 1.3 million people "kick the habit" each year, some 30 percent of the adult population continue to smoke. Approximately one million people start smoking each year. One reason some smokers refuse to quit is weight

control. Evidence shows that many smokers do gain weight after quitting. It comes as little surprise then, that smokers as a group, are relatively lean.

This latest research, conducted by GRC scientists, Dr. Hiroshi Shimokata, Denis C. Muller, and NIA's clinical director, Dr. Reubin Andres, involved an in-depth analysis of the smoking histories and body measurements on 1122 men, aged 19 to 102 years, all volunteers in the Institute's Baltimore Longitudinal Study of Aging (BLSA). Participants visited the GRC regularly to undergo a battery of physiological and behavioral tests.

The GRC investigators used waist and hip circumferences and the waist-hip ratio (WHR) as parameters to assess body fat. All measurements were taken in a standing position. To adjust for height, the body mass index (BMI) was computed and the weight divided by the square of the height. An adjustment was also allowed for age.

The findings of the study have unexpected and important clinical implications for the smoking public. While total weight and BMI proved lower among smokers when compared to nonsmokers, the circumference of the waist and the WHR in smokers was greater in the cigarette smokers than the nonsmokers. This variance increased proportionately with the actual number of cigarettes smoked daily.

Further, the scientists report that despite a modest increase in weight among smokers who quit, the increase in WHR was less than would have been anticipated. Those participants who started smoking during the course of the study experienced a decline in total body weight (on the average) but their WHR increased. Thus, cigarette smoking influenced the placement of fat in the body.

Previous studies have demonstrated that when body fat accumulates primarily around the waist, individuals greatly increase their risk for developing cardiovascular disease. In addition, experts have noted a marked propensity for developing diabetes when the waist-hip ratio is high. This is an especially important finding for older people because the incidence of diabetes and heart disease increases with age.

The investigators conclude that people who continue to smoke in order to control their body weight are making a doubly bad bargain with their health.

Scientists Explore Mechanism for Resetting the Human Biological Clock

Insomnia and other problems getting a good night's sleep are common complaints among older people. Now, scientists supported by an NIA grant have found that carefully timed exposure to bright lights might prove a quick and effective treatment for certain sleep disorders.

Drs. Charles Czeisler, Richard Kronauer, and their colleagues at Brigham and Women's Hospital and Harvard University report that the body's internal clock is more sensitive to light than previously thought and can be "set" by scheduled exposure to light over a relatively short period of time.

Located in the brain's hypothalamus, this internal clock, or circadian pacemaker, controls when we sleep and when we wake, as well as a variety of other bodily activities that influence the way we think, feel and function. Each day, the pacemaker--which runs on a cycle of about 25 hours--is reset to fit the 24-hour cycle of the calendar day. Dr. Czeisler and his colleagues have found that light may be the single most important factor in resetting the clock and that the timing of light exposure determines the extent and direction of the change.

As part of their research, the investigators conducted a total of 45 trials in 14 healthy young men. For an average eight-day trial, each participant lived in a laboratory environment devoid of all external time cues. For the first two days of the trial, the participants were kept awake while the investigators performed tests of body temperature, kidney function, alertness and performance to determine the normal setting of their pacemakers. They then experienced three days of alternating light (16 hours) and darkness (8 hours). For 5 hours during each light cycle the volunteers sat facing a bank of specially-designed fluorescent lamps with an intensity comparable to sunlight just after dawn.

As a result, the investigators found that the human circadian pacemaker can be reset to any desired phase by scheduled exposure to light for 2 to 3 days. More importantly, they found that the same exposure at different times can have significantly different effects. For example, exposure at one time in the cycle resets the clock to an earlier hour (i.e., an eastward time shift), while exposure at a different time resets the clock to a later hour (i.e., a westward time shift). Exposure at certain times causes very little effect. As part of his work on this project, Dr. Kronauer has developed a mathematical model to predict the body's response to any light exposure.

It has been known for some time that the internal clocks of animals and lower organisms are set by daily cycles of light and darkness. Scientists have long felt that in humans, social contacts and other environmental cues play a more significant role than light-dark cycles.

In 1986, Dr. Czeisler and his colleagues reported the first evidence that daily exposure to sunlight might be the key to resetting the biological clock. As part of an experiment designed to adjust slight abnormalities in circadian function, the investigators found a dramatic light-induced shift in the biological clock of a 66-year old woman who was having difficulties with her sleep.

The recent findings indicate that a schedule of alternating light and darkness can be designed so that persons can be alert whenever they need to be. This research has broad implications for people who suffer from jet-lag (some of whom require more than a week to adjust to a new schedule), for those who do rotating-shift work, and for those who suffer from insomnia.

The research also has implications for older people. According to Dr. Czeisler and his colleagues, the circadian pacemaker gradually speeds up as a person ages. Over time this could lead to early morning awakenings and other sleep complaints reported by some older people. The NIA-supported scientists have already begun to apply their findings to treat some common sleep-related complaints of older patients and are encouraged by their preliminary results.

Exercise Prevents Disabling Bone Loss in Older Women

Each year osteoporosis causes 1.5 million fractures of the wrist, spine, hip, and other parts of the skeleton in people over age 45. This bone-thinning condition, which affects more women than men, develops silently over a period of many years. Gradually and without discomfort, bone loss occurs, leading to a weakened structure less able to support normal daily activities. A minor fall or blow that would not injure most people can easily break one or more bones in someone with severe osteoporosis. Fractures directly related to osteoporosis cost Americans an estimated 7 to 10 billion dollars annually.

NIA grantees have found that exercise deters the bone loss leading to osteoporosis. Dr. Everett L. Smith and colleagues at the University of Wisconsin in Madison studied the benefit of a 4-year exercise program in previously inactive women between 35 and 65 years of age (with an average age of 50). Although women at a specific age, few have followed the effects of exercise in the same women over a period of many years. Researchers believe that early prevention of bone loss could greatly reduce the number of fractures later in life.

Before entering the study, each participant had a thorough physical examination, including measurements of bone mass and a treadmill test to assess her level of fitness. The 62 women in the control group did not participate in any organized exercise program, but continued their normal daily activities. The 80 women in the exercise group participated in a 45-minute exercise program 3 times a week.

Each exercise session included a warmup period, 25 minutes of aerobic exercise (dancing, walking, or jogging), and a cooldown period. During the first year of the study, exercises were designed primarily to increase participants' aerobic capacity. During successive years, light wrist weights, push-ups, and various dance routines that strengthen the upper body were added.

Dr. Smith measured bone width and bone mass in both forearm bones and in the upper arm bones. Measurements were taken every 3 months during the first year and every 6 months for the next 3 years. He found that bone width and bone mass declined significantly in all three bones of both arms of the participants in the control group. The rate of decline was significantly less in the exercise group.

To determine if menopause influenced the response to exercise, Dr. Smith analyzed premenopausal and menopausal participants separately. As a woman passes through menopause, her body produces less estrogen. This hormone influences bone mass by slowing or halting bone loss. As the level of estrogen drops, bones become less dense. Dr. Smith found that premenopausal and postmenopausal women who exercised did not lose as much bone mass as did the women who did not exercise. The results of this study indicate that physical activity significantly reduces bone loss in middle-aged women.

In related research, NIA grantee Dr. Gail P. Dalsky and coworkers at the Washington University School of Medicine in St. Louis, Missouri examined the effects of exercise on the spine. Dr. Dalsky studied a short-term exercise training program (9 months), which was followed by 13 months without exercise, and a long-term exercise training program (22 months). Participants were healthy, inactive women between the ages of 55 and 70.

At the beginning of the study, the women had a thorough physical examination, measurement of bone mass, and a treadmill test. Participants were given 1,500 mg. of calcium daily since some researchers believe that a shortage of calcium after menopause is associated with the development of osteoporosis.

The 19 women in the exercise group did weight-bearing exercises (walking, jogging, and climbing stairs) for 50 to 60 minutes 3 times a week. Dr. Dalsky found that bone mass in the lower spine increased significantly after the short-term weight-bearing exercise program and that an increase in bone mass was maintained during the long-term training program. After training stopped, bone mass reverted to what it had been at the beginning of the study, even with calcium intake staying at the level used during the study. These results suggest that exercising led to the increase in bone mass.

Although previous animal studies confirm this finding, this is the first time researchers have shown in humans that gains in bone mass during an exercise training program are lost when exercising is stopped. Dr. Dalsky's study indicates that continuous weight-bearing exercise can increase bone mass in postmenopausal women.

Future studies will investigate more specifically the exact amount and best type of exercise necessary to prevent bone loss. Additional research is also needed to develop alternative

exercise programs for people with joint and mobility problems that keep them from participating in aerobic exercises.

Urinary Incontinence in Nursing Home Residents

Nearly 1 million (over half) of the nursing home residents in this country suffer from loss of bladder control, or urinary incontinence. Tragically, few nursing home residents who are incontinent have had any type of diagnostic evaluation or treatment.

Although researchers have identified a number of different types of incontinence, surprisingly little is known about which forms of urinary incontinence are most widespread among nursing home residents. NIA grantee Dr. Neil M. Resnick at Brigham and Women's Hospital in Boston, Massachusetts has identified a previously unrecognized form of incontinence that is particularly common among frail older people.

Prior to Dr. Resnick's study, researchers believed that incontinence in nursing home residents was due almost exclusively to involuntary bladder contractions which cause urine to leak before an individual can reach the toilet. This condition is called detrusor hyperreflexia (DH). In most cases, the amount of urine lost is moderate and the amount of urine remaining in the bladder after voiding is small.

Dr. Resnick has identified a condition called detrusor hyperactivity with impaired contractility (DHIC). This form of urinary incontinence is similar to DH in that the bladder contracts involuntarily. Unlike DH, a significant amount of urine remains in the bladder after voiding. The bladder contraction empties only one-fourth to one-half of the bladder volume. Thus, in addition to causing incontinence, this condition is associated with urinary retention, which can lead to serious infections.

Dr. Resnick identified DHIC in patients in a nursing home and two hospitals. The study included 32 patients--27 women and 5 men. The nursing home residents averaged 89 years of age. The average age of hospitalized patients was 79 years. Participants had been incontinent more than 3 times per week for more than 2 months. Half of the patients had severe mental or physical disabilities.

Aside from the fact that DHIC is common among nursing home residents, it's diagnosis is important because this form of incontinence causes the bladder to retain urine. Urine retention can be especially harmful in patients taking medications that also cause the bladder to retain urine. In addition, DHIC may be easily misdiagnosed and mistreated. For example, this form of incontinence may closely mimic prostate obstruction in men and stress incontinence in women, resulting in unnecessary and potentially harmful surgery.

In a followup study of incontinence in nursing home residents, Dr. Resnick observed that the most common types were DH and DHIC. Surprisingly, he found that the types of incontinence in patients with dementia, mobility problems, or both did not differ markedly from the types of urinary incontinence in individuals without these disabilities. Thus, correctable causes of incontinence are much more common than previously believed, even in nursing home patients who are demented.

Urinary incontinence in frail older persons cannot be dismissed as merely due to advanced age, dementia, immobility, or institutionalization, although these factors may play a part. In a large number of patients, the cause or causes of incontinence can be identified, and in many cases, the condition can be significantly improved or cured. Patients should not be excluded automatically from urologic examinations and treatment simply because of age, frailty, or the fact that they are in a nursing home. If the patient's overall health makes treatment feasible, the cause of incontinence should be carefully sought.

Heat Shock Response Decreases in Older Animals

NIA intramural researchers Drs. Joseph Fargnoli, Nikki Holbrook, and their colleagues at the GRC report that the heat shock response, a selective expression of specific genes in response to heat or other types of physiologic stress, is altered in older animals. This finding could eventually help explain why older people are more susceptible to environmental stresses such as cold and hot temperatures.

The researchers studied the in vitro response of young and old rodents by comparing their expression of the HSP 70 gene family. HSP 70 is induced when animals are subjected to heat stress. The heat shock response is a universal response found in all organisms ranging from plants to animals. It involves the selective expression of a unique set of genes that protect cells against a variety of toxic and stressful conditions.

Dr. Fargnoli and his colleagues took lung cells from both young and old rodents, grew the cells in a culture, and then applied elevated temperature. Results showed that the young animals produced a higher number of cultures giving a good HSP 70 protein response than did the old rodents.

These results suggest a defect in the ability of cells from old animals to mount an adequate heat stress response, when exposed to high temperatures. Further investigations may help determine whether a defect in heat shock gene expression plays a role in an individual's physiological response to heat and environmental stress.

NATIONAL CANCER INSTITUTE

Cancer incidence increases with increasing age. Although aging is not the cause of cancer, the two processes are related. More than 80 percent of all cancers occur in persons age 50 and older, and 58 percent occur in people age 65 and over.

This year the National Cancer Institute (NCI) contributed to advances in health care for older people through a number of research projects, educational programs, and intervention efforts.

Early Detection of Breast Cancer

In 1989, about 142,000 new cases of breast cancer will be diagnosed in the U.S. and 43,000 women will die from this disease. Cancer Statistics Review 1973-1986, published by NCI in May, 1989 showed that during the 14-year period of the report, the incidence rate for breast cancer in women age 50 and older was nearly 10 times higher than in younger women. During the same period, the mortality rate from breast cancer in women age 50 and older increased 5 percent compared to a 9 percent decrease for women younger than 50.

Early diagnosis improves survival and mammography is the most effective way to detect breast cancer in its earliest stages. However, the 1987 National Health Interview Survey revealed that only 17 percent of U.S. women age 40 and older had a screening mammogram during the previous year. Therefore, NCI has engaged in many activities to encourage women age 40 and older to get periodic mammograms, have an annual breast exam by a physician, and perform monthly breast self-examinations.

This year 11 health care and medical research organizations, including NCI, issued breast cancer screening guidelines stating that asymptomatic women between ages 40 and 50 should have an annual clinical breast examination with mammographic screening every 1 to 2 years. Beginning at age 50, both the clinical examination and mammography should be performed yearly. Scientists estimate that breast cancer deaths would decline by at least 30 percent if women followed these guidelines.

Breast Cancer Treatment

In the area of breast cancer treatment, three NCI-funded clinical trials reported that many women with node-negative (no spread to underarm lymph nodes) breast cancer may benefit from adjuvant treatments (chemotherapy or hormonal therapy after primary treatment). Each year about half of all patients diagnosed with breast cancer have node-negative disease.

Two of the trials were conducted by the NCI-funded National Surgical Adjuvant Breast and Bowel Project, chaired by Dr.

Bernard Fisher at the University of Pittsburgh in Pennsylvania. Twenty-five institutions collaborated in one of the trials and 52 institutions collaborated in the other.

The third NCI-funded trial was a collaborative effort of the Eastern Cooperative Oncology Group, the Southwest Oncology Group, and the Cancer and Leukemia Group B. The study was chaired by Dr. Edward Mansour at Case Western Reserve University in Cleveland, Ohio.

The results provided the impetus for a "Clinical Alert" issued to physicians when the data first became available and prior to their publication in a journal. A followup assessment of the alert revealed that 75 percent of responding physicians had changed their treatment practice as a result of information provided.

Using data on more than 125,000 women diagnosed with breast cancer from 1973 to 1984, intramural researchers Dr. Rosemary Yancik and Lyn Ries, and Dr. Jerome Yates at Roswell Park Memorial Institute in Buffalo, New York studied the influence of advancing age on breast cancer. They found that 43 percent of newly diagnosed cases occur in women age 65 or older, that older women are more likely to present initially with more advanced cancers, that older women tend to have less extensive surgery than younger women, and that older women live as long as younger women after treatment for localized and regional stage disease. However, for distant disease, older women do much worse.

Replacement Hormone Therapy

NCI visiting scientist Dr. Leif Bergkvist at the Unversity Hospital in Uppsala, Sweden, intramural researchers Drs. Robert Hoover and Catherine Schairer and their colleagues conducted a study of 23,244 Swedish women who used replacement hormones (both estrogen and estrogen-progestin combinations) to ease symptoms of menopause. They reported that the risk of breast cancer was increased by 70 percent among those who had used estrogens for more than 9 years. Few women in this study used conjugated estrogens (the form most commonly used in the United States) so a risk estimate for this type of therapy could not be determined by this study.

Prostate Cancer Treatments

Found primarily in men age 50 and older, prostate cancer becomes increasingly common with each decade of life. In 1989, an estimated 103,000 new cases of prostate cancer will be diagnosed in the United States and 28,500 men will die from the disease. It is the third leading cause of cancer death in men.

Based on the results of an NCI-funded clincial trial, the Food and Drug Administration this year approved the use of a combination drug therapy (flutamide and leuprolide) for advanced

prostate cancer. The study showed that individuals with advanced prostate cancer who were treated with the drug combination survived nearly 25 percent longer than men treated with leuprolide alone.

Collaborating on this study were intramural researcher Dr. Andrew Dorr; Dr. David Crawford and Marilyn Davis at the University of Colorado in Denver; Dr. Mario Eisenberger at the University of Maryland Cancer Center in Baltimore; Dr. David McLeod at the Walter Reed Army Medical Center in Washington, D.C.; Dr. Joseph Spaulding at the University of California in San Francisco; Dr. Ralph Benson at the Mayo Medical School in Rochester, Minnesota; and Dr. Brent Blumenstein and Phyllis Goodman at the Fred Hutchinson Cancer Research Center in Seattle, Washington.

In 1989 intramural researcher Dr. Charles Myers and his colleagues at the NIH Clinical Center in Bethesda, Maryland, reported preliminary findings showing that the anticancer drug suramin produced tumor regression in 50 percent of a group of advanced prostate cancer patients who had failed standard therapy.

NCI-funded phase II clinical trials of suramin at NCI and three other institutions are attempting to confirm the 50-percent reduction. Current hormonal therapy yields a similar response rate (40 percent), however, patients often relapse within 18 months and die following 6 to 10 months.

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NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

The National Heart, Lung, and Blood Institute (NHLBI) supports and conducts research as it relates to normal function and diseases of the heart, blood vessels, lungs, and blood.

Protein Oxidation Correlated with Aging Process

Dr. Earl Stadtman, an NHLBI intramural scientist, has shown that oxidation of proteins (i.e., increasing the positive charges on the atoms) at specific sites and by specific reactions marks those proteins for subsequent selective degradation and disposal by protein-decomposing enzymes, or proteases, in cells. In Dr. Stadtman's studies, the amount of oxidized proteins in the livers of rats increased with age over a period of 2 to 26 months and this accumulation of oxidized proteins was paralleled by a decrease in selective protease activity. These findings suggest that a progressive loss of ability to degrade the oxidized proteins is the reason for their accumulation. Oxidized proteins also are present in much higher concentration in the tissues of older people, possibly because of a similar mechanism.

In related studies Dr. Stadtman found that accelerated oxidation of proteins occurs in rats exposed to higher-than-normal levels of oxygen, in gerbil brains damaged by interruption of blood flow and subsequent reintroduction of blood, and in damaged rat brains when low sodium levels are corrected. A single injection of bacterial endotoxin into rats provided a fivefold increase in the life span of animals exposed to 100 percent oxygen. The correlation of protein oxidation with age and the basic understanding of the mechanisms by which this occurs may further understanding of the aging process.

Aging Affects Diaphragm Contractility in Hamsters

The potential importance of respiratory, chiefly inspiratory, muscle fatigue has been recognized only for the last decade. If inspiratory muscles fail, so do lung ventilation and tissue respiration. There are theoretical reasons to postulate inspiratory muscle failure in chronic obstructive pulmonary disease (COPD), and there is fairly good evidence that respiratory muscle fatigue is important in certain neuromuscular diseases such as polio, amyotrophic lateral sclerosis, muscular dystrophies, and myopathies (muscle diseases).

To learn how aging affects diaphragm function, Dr. Steven G. Kelsen, a grantee at Temple University in Philadelphia, Pennsylvania studied diaphragm contractility in young adult, middle-aged, and old hamsters. Using in vitro tests on muscle strips, Dr. Kelsen showed that the maximum active tension that could be developed by the diaphragm muscles from older animals was significantly less than that developed by young adult and middle-aged animals. In addition, other changes in the measures

of muscle function were adversely affected by aging, such as the speed at which the muscle was capable of shortening. Dr. Kelsen concluded that aging adversely affects the tension-generating ability of the diaphragm, its velocity of shortening, and its resistance to fatigue.

For healthy older humans, these results are probably of little importance, since the respiratory system normally has considerable reserve. However, for those with respiratory problems such as COPD, these findings show that aging in and of itself is likely to increase the risk of developing respiratory failure due to respiratory muscle fatigue.

Aging Shown to Affect Smooth Muscle Cell Proliferation in Artery Wall

Dr. Babette B. Weksler, a grantee at Cornell University Medical College, in New York City has been studying the influence of aging on the development of arteriosclerosis in experimental animals. According to one hypothesis, the early stages of arteriosclerosis are characterized by the proliferation of smooth muscle cells (SMC) in the artery wall at sites of injury to the cells that line the vessel. Such proliferation is stimulated by growth factors (for example, platelet-derived growth factor) and slowed by growth inhibitors (for example, heparin). Dr. Weksler has shown that, following experimental injury to the vessel lining, SMC from the aortas of aged animals proliferate at a greater rate than those from young animals, and the proliferation of old vascular SMC is less dependent on serum or added growth factors than that of young vascular SMC. Aging thus favors the development of arteriosclerosis by releasing SMC from the constraints on proliferation found in the cells of young arteries.

NATIONAL INSTITUTE OF DENTAL RESEARCH

Major new efforts to assess the oral health of adults and older Americans are being supported by the National Institute of Dental Research (NIDR). Underpinning these efforts are data from the NIDR National Survey of Oral Health in U.S. Employed Adults and Seniors: 1985-1986 showing that toothlessness, root cavities, gingival (gum) bleeding, and severe periodontal destruction (i.e., destruction of the tissues surrounding the tooth) are significant problems among Americans 65 and older.

NIDR Develops Research and Action Program

Based on these findings, NIDR has developed a new initiative to improve the oral health of adult Americans. The goal of this program is to eliminate tooth loss and prevent further deterioration in individuals who have compromised dentition. The effort is being coordinated with other Federal agencies and professional and private groups.

New Understanding is Gained on Patterns of Tooth Loss

Intramural scientist Dr. L. Jackson Brown and Dr. Lawrence H. Meskin at the University of Colorado Health Sciences Center, in Denver have found that all socio-demographic groups of older people experience extensive tooth loss but that people age 65 to 69 with higher incomes have less severe tooth loss than do older people with low incomes. These differences diminish with increasing age--half of the people over 80 have no teeth.

In a related intramural study, Dr. Brown, Ms. Janet A. Brunelle, and Dr. Galen B. Warren collaborated with Dr. Meskin to present a new approach for describing tooth loss patterns. This typology will help target oral health promotional efforts.

Preliminary Data Show No Age Difference in Sensory Function

Dr. Marc W. Heft, an NIDR grantee at the University of Florida in Gainesville reports preliminary data showing for the first time that the perception of temperature in adults age 65 and older without neurological disease does not differ from that in adults age 20 to 30. This research is being coordinated with other studies at Gainesville--the site of NIDR's first Research Center on Oral Health in Aging.

Decreased Food Enjoyment is Not a Normal Part of Aging

Based on a study of men and women between ages 25 and 92, intramural scientists Drs. James M. Weiffenback, Carloyn A. Tylenda, and Bruce J. Baum have shown that oral sensory function (in terms of food enjoyment) remains intact well into old age.

Impaired Salivary Function is Associated with Alzheimer's Disease

NIDR and NIA intramural scientists Drs. Jonathan A. Ship, Charles DeCarli, Robert P. Friedland, and Bruce J. Baum report that saliva flow rates from the submandibular salivary gland, located below the lower jaw, were significantly lower among patients with early Alzheimer's disease compared to age-matched healthy individuals.

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducts and supports research into the causes, treatment, and prevention of many of the most serious chronic and disabling diseases that affect public health. Among the diseases under research that disproportionately affect older people are noninsulin-dependent diabetes and osteoporosis.

Relationship Between Noninsulin-Dependent Diabetes Mellitus and Diet Studied

The ideal diet for people with noninsulin-dependent diabetes mellitus (NIDDM), which affects about 10 million Americans who are middle-aged or older, has been a subject of controversy. Because people with NIDDM are at increased risk for coronary heart disease, most doctors recommend a low-fat, high-carbohydrate diet to help control the level of low-density lipoprotein (LDL) in the blood. LDL, the "bad" cholesterol, is associated with an increased risk of heart disease.

NIDDK grantee Dr. Roger H. Unger and his colleagues at the University of Texas Southwestern Medical Center at Dallas and the Veterans Administration Medical Center in Dallas compared the effects of both a high-carbohydrate diet and a diet high in monounsaturated fatty acids. Ten patients (mean age of 56) with NIDDM receiving insulin therapy participated in the study.

The high-carbohydrate diet provided 60 percent of calories in the form of carbohydrates and 25 percent of calories in fat. The high monounsaturated fat diet had 50 percent fat and 35 percent carbohydrates. Both diets provided comparable levels of protein, cholesterol, and dietary fiber. The researchers found that the high monounsaturated fat diet lowered blood sugar levels and reduced most patients' daily insulin requirements. This diet also raised levels of high-density lipoproteins (HDL), the "good cholesterol," by 13 percent. There was no significant difference in total cholesterol and LDL cholesterol in patients on the two diets. Preliminary results suggest that eating a diet high in monounsaturated fats, as a partial replacement for carbohydrates, may improve blood sugar control without raising blood cholesterol. Dr. Unger and his colleagues conducted this research at a General Clinical Research Center supported by NIH's Division of Research Resources.

Decreased Vitamin D Related to Osteoporosis

NIDDK-supported investigators at Columbia University in New York City have demonstrated that decreased production of the active form of vitamin D is related to both osteoporosis and aging. The researchers have established that this active form of vitamin D normally is produced by the kidney and is regulated by parathyroid hormone and by phosphate levels. Detailed information on this study can be found in the NIDDK contribution to a separate report on Arthritis, Rheumatic Diseases, and Related Disorders.

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

As people age they become increasingly susceptible to diseases of the nervous system. As the focal point for research on these diseases, the National Institute of Neurological Disorders and Stroke (NINDS) supports and conducts investigations of conditions affecting the aging population: Parkinson's disease, Alzheimer's disease, and stroke. (NINDS research on th latter two disorders is described in separate reports.)

Nearly half a million people in the United States, most over age 60, have Parkinson's disease, which is characterized by uncontrollable tremors, rigidity, and difficulties with movement and speech. These symptoms result from the loss of dopamine, a chemical messenger, from the brain's substantia nigra (located in the brain stem). They can be controlled by medication such as levodopa. Many patients however react unpredictably to such drugs. An estimated one-third to one-half of patients wht Parkinson's disease also develop dementia.

NINDS-supported scientists are studying the biological progression of Parkinson's disease and experimenting with treatment methods other than drugs.

Exploring Implant Treatment

MPTP models are also used to test treatments for Parkinson's disease, such as implants of dopamine-producing adrenal or fetal tissue into the brain. More than 100 human patients in a number of countries have already had such implants. The results have been contradictory, but varying degrees of recovery have been reported. Scientists are focusing on animal studies because it is not clear how--or whether--implants stimulate dopamine production. The grafts themselves may produce the chemical or they may encourage repair of the host's damaged dopamine system. It could also be that surgery itself stimulates repair.

An NINDS-supported team at three institutions, working with an MPTP model in African green monkeys, has found that transplants of fetal tissue from the monkey brain's substantia nigra lead not only to dopamine production but also, apparently, to functional improvement. Scientists led by Dr. Donald Redmond at the Yale University School of Medicine in New Haven, Connecticut found that the grafts significantly reversed even major behavioral abnormalities such as cognitive and motor decrements.

While many scientists believe that fetal tissue is the more promising trigger for dopamine production, some continue to work with adrenal implants. Because adrenal implants are taken from the participant's own body, they will not be immunologically rejected.

An NINDS-supported team, led by Dr. Don Gash at the University of Rochester Medical Center in New York is investigating whether adrenal grafts produce growth factors that encourage regeneration. While the grafts themselves survive poorly in the basal ganglia (a portion of the forebrain helping with voluntary movement), the team found that the procedure does encourage vigorous recovery of the remaining dopamine-producing cells in the Cebus monkeys.

Drug Trial Yields Promising Results

This year a major NINDS-supported study revealed that treatment with the drug deprenyl delays the progression of symptoms in patients with early Parkinson's disease and postpones the need for L-dopa therapy. Although scientists are unsure how deprenyl works, they believe that this is the first treatment to actually slow the progress of a neurodegenerative disorder. By contrast, therapies like L-dopa alleviate symptoms without slowing the destruction that causes them.

In the deprenyl study, the largest clinical trial ever conducted for Parkinson's disease, scientists studying 800 patients at 28 centers found that during the first year of treatment, 44 percent of 401 patients receiving an inactive placebo declined to the point of needing L-dopa to maintain their normal activities of daily living, while only 24 percent of 399 patients given deprenyl required L-dopa. These results are so promising that scientists are continuing to investigate if other positive effects are seen with longer use of deprenyl. Thus far the study has shown that patients taking deprenyl are able to continue working fulltime longer than those given a placebo.

The study, under the leadership of grantee Dr. Ira Shoulson at the University of Rochester in New York, continues to investigate the value of alpha-tocopherol (vitamin E) therapy in conjunction with deprenyl, as well as the effectiveness of deprenyl combined with L-dopa. Although there is speculation that deprenyl may be effective in other brain disorders such as Alzheimer's disease, there is no evidence or even indication at the present time that this is true.

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Older people may be more susceptible to organisms that cause bacterial and viral infections than those in other age groups. Therefore, improved ways of preventing and treating these illnesses can be lifesaving. The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports research on the biology of many of these organisms, as well as research aimed at preventing these infections.

Bacterial Pneumonia May be Acquired in Hospitals

Recently a new strain of chlamydial bacteria, called TWAR, has been identified as one cause of respiratory tract infections associated with pneumonia. The TWAR organism has been found more commonly in patients with pneumonia than in patients with other respiratory illnesses such as sinusitis.

NIAID grantee Dr. J. Thomas Grayson and his colleagues at the University of Washington in Seattle conducted a retrospective study of the relationship between TWAR and pneumonia. The researchers looked at patients who entered the hospital with pneumonia and those who developed pneumonia during their hospital stay. Most of the patients ranged in age from 55 to 60 years old and most had a chronic illness such as heart disease.

Dr. Grayson and his colleagues looked for an antibody to TWAR in samples of the patients' blood. (An antibody is a protein in the blood that attacks foreign organisms.) They found that 10 percent of the 198 hospitalized patients had TWAR antibody levels indicating of recent infection. When compared with 20 control cases of pneumonia, there was no difference in symptoms or clinical signs of pneumonia. Nine of the 20 TWAR patients acquired pneumonia in the hospital.

The study demonstrates that TWAR-associated pneumonia can be acquired in the hospital as well as in the community. It also confirms studies showing that community-acquired TWAR-associated pneumonia in patients with chronic illnesses can result in clinical complications and even death. Futher studies will determine percisely how TWAR is transmitted in the hospital--whether it is spread only by person-to-person contact, as is common in the community, or whether a reactivated TWAR infection may be responsible. This study is another step toward determining what role TWAR plays in causing pneumonia.

Effects of Drugs on Herpes Zoster Are Studied

Chickenpox, which is caused by a type of herpes virus called varicella-zoster, is contracted by most people during childhood. After the infection has subsided, the virus becomes dormant, remaining in the body but causing no ill effects. However, varicella-zoster virus sometimes reactivates later in

life, causing herpes zoster, also known as shingles. It has been estimated that about 50 percent of people who live to age 80 will have an attack of shingles.

Symptoms of herpes zoster can range from mild itching to intense pain. Herpes zoster can result in blindness if it affects the eyes. In people with a weakened immune system, shingles may result in disseminated disease in which the virus spreads to organs throughout the body. It can also be life threatening.

NIAID contractor Dr. Richard J. Whitely at the University of Alabama in Birmingham directs the NIAID Collaborative Antiviral Study Group, which is investigating the effects of acyclovir (an antiviral drug) and prednisone (an anti-inlammatory drug) on herpes zoster. They are studying these drugs alone and in combination. Acyclovir has already been shown to be beneficial against herpes virus infections. The study group is also comparing intravenous vidarabine (another antiviral drug) with acyclovir for treating disseminated herpes zoster in immunocompromised patients. In addition, they are investigating whether oral acyclovir will prevent the spread of shingles in immunocompromised patients who have localized infection. It is hoped that these studies will soon provide a way to relieve the debilitating symptoms of herpes zoster.

NATIONAL EYE INSTITUTE

Americans 65 and older account for one-third of all visits for medical eye care. The National Eye Institute (NEI) supports research aimed at reducing the burden of aging-related eye disease.

Scientists Study Treatment for Glaucoma

Open-angle glaucoma, the most common form of glaucoma in this country, is a leading cause of blindness in Americans 65 and older. Although its cause remains unknown, glaucoma occurs when the natural flow of fluid inside the eye becomes blocked, leading to a buildup of internal pressure that damages the optic nerve.

Most cases of glaucoma can be controlled with medication, but for some the medications become ineffective or intolerable. The next step is a filtering surgery to create a drainage channel to relieve the pressure. In some surgical patients, however, scar tissue later obstructs the drainage channel necessitating a second operation, which often fails. In addition, patients who have had cataracts removed are poor risks for successful filtering surgery.

Early findings from an NEI-sponsored randomized, controlled, clinical study show that patients who have had glaucoma or cataract surgery have almost a 50 percent better chance of successful surgery if it is followed by injections of an antimetabolite drug called 5-fluorouracil, or 5-FU. The drug impedes the growth of scar tissue. When the superior results of the combination therapy became evident, the investigators stopped the randomization and reported on the condition of all patients one year after surgery.

Of the patients who received 5-FU after surgery, 73 percent had filtering channels that were still maintaining satisfactory intraocular pressure after one year, while only 50 percent of those who had surgery alone had the same results. Although the 5-FU injections caused some mild and transient side effects in the first month after surgery, two-thirds of those receiving the drug did not need glaucoma medication to control their intraocular pressure. In the surgery-alone group, only about one-third maintained satisfactory pressure without medication. Moreover, of the patients needing medication after surgery, those in the 5-FU group needed fewer types of medications than did those who had surgery alone.

Although patient status after 1 year is a good predictor of long-term results, the investigators plan to follow the patients for 5 more years to determine how the surgical filters in the eyes of both groups continue to function.

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) conducts and supports research on several diseases that affect older Americans, particularly osteoporosis and osteoarthritis.

Researchers Study Osteoporosis

Dr. Carl T. Brighton and his colleagues at the University of Pennsylvania in Philadelphia have applied a novel approach to study the use of electrical stimulation to treat osteoporosis in an animal model. Electrical stimulation is a technique developed by Dr. Brighton and others in which fractures that fail to heal are subjected to low-level electric fields and currents to stimulate the rate of bone growth and repair. Using this technique on rats, the researchers were able to increase bone mass in the lower limb and to reverse osteoporosis of the spine. This innovative research offers hope that loss of bone mass in osteoporosis can be reversed.

In other osteoporosis research, intramural scientist Dr. Mark E. Bolander and his colleagues have developed a method for evaluating the effect of estrogen on bone formation. Recent research has shown that bone cells contain binding sites for estrogen, called receptors, that attach to DNA in the cell. Using advanced molecular biology techniques, Dr. Bolander and his colleagues found that the level of estrogen receptor varies during fracture healing, implying that estrogen has a direct effect on bone formation. Increased knowledge about molecular action of estrogen during bone formation and healing should add signficantly to researchers' understanding of osteoporosis and other bone disorders and, ultimately, to the ability of physicians to treat these disorders.

Early Osteoarthritis May Be Linked to a Genetic Abnormality

Osteoarthritis (OA) or degenerative joint disease is usually thought of as an inevitable part of aging. However, new studies show that in some families, where there is no identifiable cause for the disease, OA may be linked to a genetic abnormality.

NIAMS grantees Dr. Darwin J. Prockop at Jefferson Medical College in Philadelphia, Pennsylvania and Dr. Roland W. Moskowitz at Case Western Reserve University School of Medicine in Cleveland, Ohio studied three generations of family members with primary OA who exhibited symptoms of the disease in their early 20s and 30s. After physical examinations and laboratory studies of these patients, the researchers ruled out other diseases. However, X-rays revealed abnormalities of multiple joints typical of primary OA and mild chondrodysplasia (abnormality of cartilage) in the spine. Blood cells from these patients were

evaluated and genetically mapped. In each of these patients the researchers found a defect in or near the gene for type II procollagen, the precursor for collagen, the major structural protein of cartilage. According to the researchers, this defect may account for the early onset of this unique type of OA. This work may also help researchers understand causes of OA in older Americans.

Additional findings relevant to disorders that affect older people can be found in the NIAMS report on Arthritis, Rheumatic Diseases, and Related Disorders.

NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS

Today more than half of the population age 65 and older are significantly affected by a communication disorder. Research into the effects of advancing age on hearing, vestibular function (balance), speech, voice, language, and chemical and tactile senses, is a major concern of the National Institute on Deafness and Other Communication Disorders (NIDCD). Created in October 1988, NIDCD currently manages a research portfolio in the communication sciences/disorders that has been primarily transferred from NINDS.

Hearing Problems Common in Older People Studied

Presbycusis (the loss of ability to perceive or discriminate sounds as a part of the aging process) is a prevalent but understudied disabling condition. In presbycusis, the inner ear is primarily affected although auditory nerve and brain stem degeneration may also occur. One-third of people 65 years and older have presbycusis sufficient to interfere with speech perception. The prevalence rises with increasing age.

Studies of the influence of factors such as genetics, noise exposure, cardiovascular status, systemic diseases, smoking, diet, personality, and stress types are contributing to a better understanding of the condition. The effect of known tissue changes combined with the cumulative effect of years of exposure to toxic influences is also being investigated.

Studies are identifying the contributions of varying aspects of presbycusis to the actual problems of speech, language, and understanding. This research is providing new information about structural, functional, and chemical changes in the aging auditory system. Anatomical and physiological studies are transferring new techniques from cellular and molecular biology to develop animal models for presbycusis. Clinical intervention research is aimed at detection, measurement, and rehabilitation (including hearing aid use).

Researchers have recently discovered that hair cells in the cochlears of both young and adult birds can regenerate if they have been damaged by toxic drugs or noise exposure. In some fish, the vestibular hair cells are replenished almost continuously throughout the life cycle. NIDCD researchers are studying these regenerating hair cells to define the biochemical and genetic mechanisms that initiate the regeneration process.

DIVISION OF RESEARCH RESOURCES

At research facilities across the United States, the Division of Research Resources (DRR) supports and conducts research into the process of aging. Through its General Clinical Research Center (GCRC) program, DRR provides the research infrastructure for multidisciplinary studies on both children and adults. Specifically, DRR provides patient research facilities, computerized data management and analysis, as well as research nurses, dietitians, biostatisticians, and specialized laboratories for the translation of basic and clinical research into medical practice.

New Research Directions in Osteoporosis

One area of intense study is osteoporosis, especially among postmenopausal women. Studies conducted by DRR grantee, Dr. John Bilezikian and associates at the Columbia University GCRC in New York City have traced the weakening of osteoporotic bones in part to a possible abnormality in the parathyroid gland, which plays a role in regulating calcium in the bone. Dr. Bilezikian has demonstrated that the parathyroid's response is diminished in postmenopausal women who have osteoporosis.

Dr. Bilezikian administered phosphate to 8 postmenopausal women with osteoporosis and 10 women of similar age who showed no signs of the disease. Phosphate, which stimulates the parathyroid to secrete a hormone that increases bone calcium, produced a strong response in the women without osteoporosis and a weak response in women with osteoporosis. The finding indicates that a defect in the parathyroid gland might contribute to osteoporosis. Future research should examine how to improve the capacity of the parathyroid gland to compensate for the loss of calcium in patients with osteoporosis.

Spinal osteoporosis, a disease characterized by progressive loss of bone in the spine, affects about 5 million Americans, most commonly postmenopausal women. Because the bone loss weakens the spinal vertebrae, patients are susceptible to fractures of the spine, which can result in curvature of the back, back pain, and gastrointestinal distress. About one-half million persons suffer these fractures each year. Now, Dr. Charles Y.C. Pak, DRR grantee from the University of Texas Southwestern Medical Center GCRC in Dallas has conducted clinical tests which point to a new treatment to increase bone mass.

Dr. Pak's treatment combines a slow-release form of sodium fluoride with a calcium citrate supplement--a combination that increases bone mass and remineralizes bone. Conventional therapy, using estrogen and calcium supplements, prevents the development of osteoporosis when applied early in the postmenopausal period. The new treatment can help patients who have already sustained substantial bone loss.

In a multicenter trial led by the Texas GCRC, more than 300 patients were monitored for an average of 3.5 years. Following the new treatment, bone density in the lower spine stabilized or increased. Patients showed an average annual increase of 5.1 percent in bone mass for up to 4 years of study. Using bone biopsies, the researchers documented an increase in the amount of normally mineralized bone which was mechanically intact or improved. Adverse complications of treatment were minor; fewer than 5 percent of patients had gastrointestinal complications and only about 6 percent experienced rheumatic complications--none resulting in stress fractures.

Amino Acids Found to Influence Absorption of Levodopa

Parkinson's disease is another common disorder in older people. Scientists have long known that its symptoms generally respond to therapy with drugs such as levodopa. Regular use of levodopa however may cause variable responses--relief of symptoms becomes neither reliable nor consistent.

Dietary protein affects the response to levodopa, but the reason why has been difficult to explain. DRR grantees led by Dr. John Nutt at the Oregon Health Sciences University GCRC in Portland analyzed the clinical response of 5 patients to meals with varying levels of protein. By monitoring the plasma level of the drug, they found that absorption of levodopa took place at the same rate regardless of the protein content of the meal. Yet the patients eating meals with the most protein showed the most fluctuations in response to the drug. Dr. Nutt concluded that the effect of dietary protein on the response to levodopa may result from elevated blood levels of amino acids derived from the digestion of dietary proteins.

These dietary amino acids compete with levodopa for entry into the brain. According to Dr. Nutt, elevated levels of amino acids in the blood can exclude the levodopa from the brain and, therefore, prevent a beneficial response. Reducing the levels of these amino acids may increase levodopa's therapeutic effectiveness.

The study of dopaminergic agents such as levodopa in Parkinson's disease is not only important because of the immediate clinical implications but also because it adds to our understanding of the brain's response to replacement therapies for neurotransmitter deficiencies. As a result, what is learned in Parkinson's disease may be important in other disorders such as Alzheimer's disease, in which the deficiency of another neurotransmitter is believed to be particularly critical.

NATIONAL CENTER FOR NURSING RESEARCH

The National Center for Nursing Research (NCNR) focuses on the causes of mental and physical dysfunction in older Americans and on ways to help older Americans maintain their physical and mental function abilities. NCNR also supports research on stress and coping associated with family caregiving and on improving methods of care at home.

Reducing the Risks of Developing Pressure Sores

Older patients in nursing homes and other chronic care facilities are at an increased risk of developing pressure sores. These sores can cause extreme discomfort to the patient and increase the risks of infection and death.

NCNR grantee Dr. Nancy Bergstrom at the College of Nursing, University of Nebraska Medical Center in Omaha is testing and refining a scale that nurses and other health care workers can use to identify individuals at high risk for developing pressure sores. Dr. Bergstrom and her colleagues are testing the scale in up to 1,100 patients in nursing homes, hospitals, and at home. The scale assesses the following factors associated with the development of pressure sores: undernutrition, reduced skin sensation, low activity levels, moisture remaining on the skin, and friction.

Dr. Bergstrom and her colleagues will also measure other conditions that might affect the development of pressure sores, such as blood pressure and skin temperature. In addition, they will look for differences in risk among racial groups.

Patients in hospitals and nursing homes will be evaluated 3 times a week; those cared for at home will be evaluated once a week.

An accurate scale to predict which patients are at highest risk of developing pressure sores can help caregivers offer prompt preventive treatment. It may also reduce the costs of care by making sure that expensive preventive measures are available to those patients with the greatest need.

OUTLOOK

The breadth of these research highlights demonstrates the remarkable opportunities available to researchers interested in aging issues. Through its research programs, the NIH is committed to implementing a research agenda that will lead to a fuller understanding of the biomedical, behavioral, and social processes that have an impact on aging. Since 1974, the NIA has been at the confluence of these research efforts.

We are an aging society--we appreciate the benefits of this longevity, but can also anticipate the drawbacks. Research conducted or supported by NIA touches the lives of each and every American. Through this comprehensive research effort we are learning more about what it means to grow old. We are seeing that aging does not have to be synonymous with decline, and we are learning that the changes we make today can improve our chances of remaining healthy, active, and independent.

HEALTH CARE FINANCING ADMINISTRATION

Services to the Aged

A. Medicaid Program

Title XIX contains several provisions directed primarily to those persons aged 65: payment of Medicare premium, copayment, and deductible amount (for each assistance recipient); and coverage of inpatient hospital services in institutions for mental diseases. Long term care services, including skilled nursing facility services used primarily by the aged, as well as prescription drugs, eyeglasses, and hearing aids, may also be covered by Medicaid.

The aged amount to a significant portion of Medicaid expenditures. About 36 percent of Medicaid program dollars will be spent on care for the aged in FY 1991, and it is estimated that 3.7 million people over age 65 (or about 14 percent of all recipients) will receive health care services. For most of these persons, Medicaid provides services which supplement and complement those provided by Medicare.

B. Medicare Program

In FY 1991, about 34.7 million persons will be covered under Medicare. Of these, 31.4 million will be persons aged 65 or over, and 3.3 million will be under age 65 but disabled. Within this Medicare-covered group, Hospital Insurance beneficiaries are protected against the costs of inpatient hospital services, skilled nursing facility services, home health services and hospice care. The voluntary Supplementary Medical Insurance program generally covers the cost of specific physician and physician-related services. Both parts of the Medicare program provide payment for the covered health services subject to certain deductibles and coinsurance amounts. a/

Under current law, Hospital Insurance program benefit payments for FY 1991 are expected to total $65.4 billion, while Supplementary Medical Insurance benefit payments are expected to be $47.9 billion.

(a) The Medicare Catastrophic Coverage Act, which would have limited these deductible and coinsurance amounts, and also provided some new health benefits, has been repealed. These Catastrophic benefits will be phased out during FY 1990.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Social Security Administration
Aging

I. OASDI BENEFITS AND BENEFICIARIES

At the beginning of 1988, about 93 percent of all Americans age 65 and over were receiving Social Security benefits or were eligible to receive benefits if they or their spouses retired; about 92 percent of the people who reached 65 in 1987 were eligible for benefits. It is expected that 93 to 95 percent of the aged will be eligible for Social Security benefits by the end of the century.

At the end of September 1989, 39.0 million people were receiving monthly Social Security cash benefits (an increase from 38.5 million in September 1988). Of these beneficiaries, 24.2 million were retired workers, 3.5 million were dependents of retired workers, 10,975 were uninsured individuals receiving "special age-72" (Prouty) benefits, 4.1 million were disabled workers and their dependents, and 7.2 million were survivors of deceased workers.

The total monthly benefits paid to beneficiaries on the rolls for September 1989 was $19.4 billion compared to $17.9 billion for September 1988. Of this amount, $14.1 billion was paid to retired workers and their dependents, $1.9 billion was paid to survivors, and $1.7 million was paid to special age-72 beneficiaries.

Retired workers received an average benefit for September 1989 of $540 (up from $516 in September 1988), while disabled workers received an average benefit of $530 (up from $509). Retired workers newly awarded Social Security benefits for September 1989 average $510, while disabled workers received average initial benefits of $540. During fiscal year 1989 (October 1988--September 1989), $227.2 billion in Social Security cash benefits were paid compared to $213.9 billion in fiscal year 1988. Of that total, retired workers and their dependents received $157.7 billion, survivors received $46.7 billion, and special age-72 beneficiaries received $23 million. In addition, lump-sum death payments amounts to $207 million.

II. SUPPLEMENTAL SECURITY INCOME BENEFITS AND BENEFICIARIES

On January 1, 1990, SSI payment levels increased by $18.00 for an individual and $26.00 for a couple. Thus, beginning in January 1990, maximum monthly Federal SSI payment levels increased from $368.00 to $386.00 for an individual, and from $553.00 to $579.00 for an eligible couple.

During fiscal year 1989 nearly $14.3 billion in benefits (consisting of $11.43 billion in Federal funds and $2.90 billion in federally-administered State supplements) were paid. Of 4.6 million beneficiaries on the rolls during September 1989, 1.4 million were aged, and 3.1 million were receiving SSI based on blindness or disability, although 579,500 of those in the latter category reached age 65 after they began receiving payments.

III. BLACK LUNG BENEFITS AND BENEFICIARIES

For September 1989, about 229,000 individuals received $72.9 million in black lung benefits which were administered by the Social Security Administration. These benefits are financed from general revenues. Of these individuals, 52,000 miners received $27.2 million, while 124,000 widows and children not in the custody of a miner or entitled widow received $45.7 million.

Black lung benefits increased by 3.6 percent in January 1990 due to an automatic general benefit increase adjustment under the law. The monthly payment to a coal miner disabled by black lung disease is $371.80. The monthly benefit for a miner or widow with one dependent is $557.70 and with two dependents is $650.70. The maximum monthly benefit payable when there are three or more dependents is $743.60.

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ALZHEIMER DISEASE
Obligations

Public Health Service:	1987	1988	1989	1990 Estimate	1991 Estimate
National Institutes of Health:					
National Institute on Aging	$42,038,000	$47,734,000	$77,729,000	$91,264,000	$94,878,000
National Cancer Institute	---	---	106,000	107,000	111,000
National Institute of Neurological Disorders and Stroke	18,611,000	18,779,000	20,990,000	21,660,000	22,657,000
National Institute of Allergy and Infectious Diseases	1,446,000	1,041,000	1,539,000	1,570,000	1,658,000
National Institute of Child Health and Human Development	583,000	671,000	741,000	775,000	800,000
National Eye Institute	62,000	---	---	---	---
National Institute of Environmental Health Sciences	327,000	575,000	595,000	615,000	678,000
Division of Research Resources	2,010,000	1,211,000	1,429,000	1,334,000	1,305,000
National Center for Nursing Research	229,000	230,000	1,853,000	2,400,000	2,400,000
Office of the Director, NIH 1/	---	66,000	---	---	---
TOTAL, NIH	65,306,000	70,307,000	104,982,000	119,725,000	124,487,000

	1987	1988	1989	1990 Estimate	1991 Estimate
Centers for Disease Control	---	103,573	154,500	155,500	171,000
Alcohol, Drug Abuse and Mental Health Administration	10,102,000	14,031,000	23,632,000	26,210,000	26,644,000
TOTAL, PHS	75,408,000	84,441,573	128,768,500	146,090,500	151,302,000
Health Care Financing Administration	523,308	77,904	1,100,000	1,000,000	1,000,000
Office of Human Development Administration on Aging	1,240,431	1,899,874	470,000	900,000	500,000
TOTAL, DHHS	77,171,739	86,419,351	130,338,500	147,990,500	152,802,000

1/ This includes AREA awards for FY 1987 - 1991, and RCMI awards for FY 1987 and FY 1991

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NATIONAL INSTITUTES OF HEALTH

National Institute on Aging

ALZHEIMER'S DISEASE

Since the mid-1970's, research on Alzheimer's disease has become a high priority for the Nation. As it has become increasingly apparent that "senility" is not a normal part of aging, investigators from many fields of science have begun to study what causes this disease and how it can be diagnosed, treated, and perhaps someday, cured.

The search for the cause of Alzheimer's disease has focused on the role of genes, toxins, infectious agents, head trauma, stress, and changes in the immune system, the endocrine system, and normal metabolic processes. Scientists are looking at each of these as possible causes of Alzheimer's disease, either alone or in combination. Others are exploring the possibility that the risk of Alzheimer's disease might be increased by age-related changes in healthy brain tissue.

The highlights presented here represent only a sample of the NIH research on Alzheimer's disease that is supported or conducted by the National Institute on Aging (NIA), the National Institute of Neurological Disorders and Stroke (NINDS), the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Child Health and Human Development (NICHD), the National Institute of Environmental Health Sciences (NIEHS), the Division of Research Resources (DRR), and the National Center for Nursing Research (NCNR). Within the Federal government, research on Alzheimer's disease is also supported by the National Institute of Mental Health, the Administration on Aging, the Health Care Financing Administration, the Centers for Disease Control, and the Veterans Administration.

Scientists Revise Estimates on Prevalence of Alzheimer's Disease

Studies done in the mid-1970's estimated that 2.5 million older Americans suffer from Alzheimer's disease. Now, NIA-supported scientists have given us reason to believe that the current number may be closer to 4 million, and that this figure may double or triple in the next century if more is not done to cure or prevent the disease.

Beginning in 1982, Dr. Denis Evans and his colleagues at Harvard Medical School in Boston, Massachusetts conducted a census of 32,000 people living in East Boston, a well-defined, stable, working-class community. More than 80 percent of the 4,485 residents over age 65 then participated in the first stage of examination by responding to a questionnaire concerning medical and social problems, and by taking a brief memory test. Of these, 467 were selected for more extensive evaluation to rule

out the presence of conditions other than Alzheimer's disease. The evaluation included a neurological examination, a brief psychiatric evaluation, laboratory tests, a brief review of medical history, and a review of current medications.

What Dr. Evans and his colleagues found was that more than 10 percent of the people over age 65 had probable Alzheimer's disease, and the prevalence of the disease rose more rapidly with age than previously suspected. Of those people between the ages of 65 and 74 years, 3 percent had probable Alzheimer's disease, as compared to 18.7 percent in the age 75 to 84 year group and a striking 47.2 percent over age 85. This translates to about 4 million Americans who might currently suffer from Alzheimer's disease.

The East Boston study is unique in several respects. First, the investigators did not look for Alzheimer patients in institutions, but rather focused their attention on people living at home, where some four-fifths of all people with dementia may live. East Boston is a particularly interesting community in this regard, because a large proportion of disabled people are cared for at home. Second, given the makeup of the East Boston community, the researchers were able to study much larger numbers of very old people than have been included in previous studies. Finally, they examined people who performed well on the initial screening test, as well as those who performed poorly. As a result, Dr. Evans thinks that he has developed the most accurate picture to date of Alzheimer's disease in the U.S. population.

Based on Census Bureau projections for the numbers of people 85 and older, Dr. Evans estimates that there could be a seven-fold increase in the numbers of oldest victims of Alzheimer's disease, contributing to a total of between 10 and 14 million people over 65 with Alzheimer's disease by the middle of the next century.

Dr. Evans and his colleagues believe that even these projections may be too conservative, in part because of assumptions that the Census Bureau has made about future numbers of older people. In making their estimates, Dr. Evans and his colleagues used the middle range of estimates provided by the Census Bureau for the 21st century. If, as some scientists have speculated, medical advances and other factors result in a greater proportion of people living to extreme old age, then the numbers of Alzheimer patients in the next century would be much higher.

Conservative or not, these figures signal the growing magnitude of Alzheimer's disease as a major public health problem over the next several decades.

Studies in China Show Surprising Differences in Dementia Rates

The future impact of Alzheimer's disease is as important an

issue in many other countries as it is in the United States. With worldwide increases in average life expectancy, both industrialized and developing nations are beginning to look at the prevalence of Alzheimer's disease and how it will affect their future.

A recent study of more than 5,000 older residents of Shanghai, China found that Chinese are just as likely to suffer from severe dementia as Americans. This contradicts previous research that suggested remarkably low numbers of Chinese suffering from Alzheimer's disease, multi-infarct dementia (caused by a series of minor strokes), or other serious dementias.

A research team including Dr. Robert Katzman, director of the NIA-supported Alzheimer's Disease Research Center at the University of California, San Diego, recently found that rates for severe dementia in one area of China are nearly identical to those found in the United States, with one exception: the rate of severe cognitive impairment is nearly three times higher for Chinese women over age 65 than for their American counterparts.

According to the investigators, this may in part be due to the very high illiteracy rates, particularly among the women, in the population they studied. It has long been known that education has a significant impact on one's ability to learn, reason, remember, and perform on tests of mental ability. It is unclear what impact compromised test performance might have had on the study results.

Future research will focus on the prevalence of Alzheimer's disease as well as other specific causes of cognitive impairment in China, and on gender differences. Such studies of Alzheimer's disease in different cultures may provide a more accurate assessment of worldwide prevalence and reveal some clues to the cause or causes of the disease.

How Common is Dementia in Black Populations?

A study of older white and black community residents of a five-county region of North Carolina has suggested that the prevalence of dementia among blacks may be distinctly greater than among whites, and that black women are particularly affected.

NIA-supported scientists Drs. Albert Heyman, Gerda G. Fillenbaum and colleagues at the Duke University Medical Center in Durham, North Carolina found that while the rate of dementia among white men and women was basically equal in this study, more than twice as many black women as black men showed signs of dementia.

This is not the first time that research has shown blacks to be more adversely affected by dementia than whites. Nonetheless,

the investigators caution that these are preliminary data that require further study. Future research will focus on how much of dementia among blacks is actually due to Alzheimer's disease and how much is related to hypertension and cerebrovascular disease.

Scientists Study How and Why Brain Cells Die

In recent years, it has become evident that the key questions in Alzheimer's disease are what causes nerve cells to dysfunction and why do specific groups of brain cells die.

Neurofibrillary tangles (tangled nerve cell fibers) and neuritic plaques (dense, insoluble deposits of a protein known as amyloid) are classic markers of Alzheimer's disease. With no way to diagnose the disease in living patients, physicians have depended upon the number and density of these lesions at autopsy to diagnose the disease. Recently, there has been a debate in the scientific community about whether these markers, particularly the neuritic plaques, signify the debris left by dying cells, or whether they mark the onset of the disease.

Some scientists, such as Dr. Donald Price, director of the NIA Alzheimer's Disease Research Center at The Johns Hopkins University in Baltimore, Maryland, think that amyloid deposits are an end stage event in the disease process. (His work is described in the NINDS section of this report.)

On the other side of the debate are NIA grantees Dr. Carl Cotman at the University of California at Irvine, Dr. Dennis Selkoe at Harvard Medical School and Brigham and Women's Hospital in Boston, and Dr. Rachael Neve and her colleagues at Children's Hospital in Boston.

This year, Drs. Cotman and Selkoe found a fragment of the amyloid protein in neuritic plaques that may possess the ability to regulate growth of nerve cells in the healthy human brain. Until now, scientists have not known what role amyloid plays, if any, in healthy brain tissue or why an increasing number of large amyloid clusters appear in the brains of Alzheimer patients.

Other NIA-supported studies have revealed that the abnormal amyloid consists of fragments of a larger protein that is normally spread across nerve cell membranes. Scientists also have discovered the approximate location of the gene for the fragment, called the amyloid precursor protein, and have identified the amino acids that constitute it.

Recently, Drs. Cotman and Selkoe synthesized the first 28 amino acids of the amyloid protein and tested the effects of this synthetic peptide on nerve cells grown in tissue culture. Usually such cells do not survive long but in the presence of the synthetic peptide, the cells stayed alive for longer periods of time. These results demonstrated that amyloid has a trophic, or growth-enhancing, effect on nerve cells.

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On the basis of these experiments, Drs. Cotman and Selkoe speculate that plaque formation in Alzheimer's disease may signal the nerve cells' attempt to mount a defense against the degenerative process and to compensate for the damage that occurs as the disease progresses.

Dr. Rachael Neve and her colleagues have found that a portion of the amino acid chain that makes up the amyloid precursor protein might be toxic to nerve cells. These investigators genetically altered (transfected) a group of tumor cells so that they contained portions of the gene for the amyloid precursor protein. They then treated the cells with nerve growth factor, which, under normal circumstances, would cause the cells to differentiate. Instead, a majority of the altered cells degenerated and died. In a second experiment, they added the transfected cells to normal cells taken from the hippocampus of rats. The hippocampus is an area of the brain that is essential for learning and memory and that is severely affected in people with Alzheimer's disease. This time, within three days, all of the brain cells had died.

Dr. Neve speculates that the amyloid precursor protein is only toxic when a portion of the peptide--the first 105 amino acids including the 28 amino acids examined by Drs. Cotman and Selkoe--is present. This suggests that altered production of the amyloid precursor protein may activate the neurotoxic peptide.

If the production of an abnormal, malfunctioning amyloid protein is among the first in a series of events that take place as brain cells begin to die, then scientists might be one step closer to finding out what causes the disease and how to cure or prevent it. More immediately, the study of amyloid may pave the way to a diagnostic test for patients who complain of serious memory loss.

Marker for Alzheimer's Disease Found in Skin

What happens when an older person begins to show signs of memory loss and confusion? With luck, someone--perhaps a relative--will realize the importance of going to a physician to find out what is causing the problem, if it is curable and, if it is not, what can be done to help. The patient's first contact with a health professional is likely to be an internist, a geriatrician, or a family practitioner. Because of the variety of conditions that can mimic Alzheimer's disease--and also because of the wide range of symptoms--the patient might be examined by a neurologist or a psychiatrist. The patient might be subjected to a complete medical examination with blood tests, laboratory tests, tests of mental status, and other specialized tests such as computed tomography or other brain scans. In the end, the diagnosis of Alzheimer's disease will be made by excluding other possible conditions. The accurate diagnosis of the disease clearly represents a challenge for physicians and often represents an emotional and financial crisis for older

people and their families.

Building upon his research in the area of amyloid, Dr. Dennis Selkoe this year announced that a simple, reliable diagnostic test may be on the horizon. Dr. Selkoe and his colleagues have found diffuse deposits of amyloid protein in the skin, the tissues just beneath the skin, and in the intestines of patients with autopsy-confirmed diagnoses of Alzheimer's disease.

The investigators examined tissue samples taken at autopsy from 11 people who had Alzheimer's disease and 26 who did not. Ten of the 11 Alzheimer cases showed some signs of amyloid outside of the brain, as compared to only three of the 26 people who had died of other causes. Those three were all older than 77 years old when they died. It has long been known that all of the hallmarks of Alzheimer's disease are seen to a lesser degree in normal aging.

In addition to this work with autopsy samples, Dr. Selkoe and his colleagues also examined tiny pieces of fresh skin taken from the forearms of an 85-year-old Alzheimer patient and a 64-year-old healthy person. The tissue from the patient contained amyloid; the other did not.

Dr. Selkoe is now looking for signs of amyloid circulating in the bloodstream. If found, it could indicate how amyloid collects in the brain of Alzheimer patients and lead to development of a blood test to diagnose the disease.

Scientists don't yet know if a test of this sort would be reliable in the early stages of Alzheimer's disease. Nonetheless, Dr. Selkoe's research supports speculation that Alzheimer's disease is not limited to the brain, as well as the theory that an abnormal form of amyloid is implicated early in the disease process. If this work is corroborated and expanded, it could be the key to diagnosing and, eventually, preventing Alzheimer's disease.

A Unifying Hypothesis for Brain Aging and Alzheimer's Disease

Even if amyloid begins to accumulate early in the course of Alzheimer's disease, something happens to trigger the event. NIA associate director Dr. Zaven Khachaturian heads a group of experts on brain aging who have offered one possible explanation.

In the quest for a common mechanism to explain what happens to the brain in healthy aging and disease, Dr. Khachaturian and others are turning their attention to an element that is essential to all plant and animal life--calcium. All cells, and neurons (nerve cells) in particular, depend on calcium to carry out their activities. Calcium not only serves as a signal that initiates such cellular activity as neurotransmitter (chemical messenger) release, but it is also needed for neuronal growth and repair, for cells to decode genetic messages, and for regulating

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proteins involved in removing cellular debris.

As noted above, the same pathology that characterizes Alzheimer's disease is also seen, to a lesser extent, in normal aged brain tissue. Some scientists would go so far as to suggest that most, if not all, people have a pre-clinical form of Alzheimer's disease and would develop the condition were they to live long enough. Whether or not this is the case, the association points to the possibility of a common mechanism at the root of brain aging and dementia.

That mechanism may involve the regulation of calcium within cells. Normally, the amount of calcium inside excitable cells such as muscle or nerve cells is very low compared to that outside the cell. To maintain these low levels, nerve cells have several mechanisms. These include channels inside the membrane that encloses the cell which allows calcium to be transported into and out of the cell. Other calcium regulators include energy-driven chemical pumps that expel excessive calcium; storage or sequestration systems that act as sponges, soaking up excess calcium; and special proteins that bind to calcium, thus preventing its activity in the cell. There is now substantial evidence that the aging process affects the efficiency of many of these calcium regulatory systems. In Alzheimer's disease these systems appear to be affected to such a degree that the normal operation of cells may be disrupted. Sudden large increases in calcium levels inside a nerve cell can lead to cell death. Investigators have now begun to speculate that even small, but sustained, disruptions of calcium balance (homeostasis) within the cell could be responsible for many of the changes that occur in normal brain aging and in Alzheimer's disease.

Numerous investigations are underway to identify calcium channels within cell membranes and see whether they behave differently with age. These membranes are composed of two layers of a fatty substance called lipids. Sandwiched inside this lipid bilayer are proteins that transport calcium into and out of the cell. Last year NIA grantee Dr. Jay Pettegrew at the Western Psychiatric Institute and Clinic in Pittsburgh, Pennsylvania found irregularities in the phospholipid compounds of lipids and phosphorous makeup of cell membranes in Alzheimer's disease. Now it has been shown in experimental artificial membranes that changes in the makeup of membrane phospholipids affect the efficiency of membrane-imbedded proteins.

Membrane irregularities may explain the changes in membrane transport function that have been observed by Dr. Mary L. Michaelis and co-workers at the University of Kansas in Kansas City. They have shown in rats that membrane transport systems clearly become less efficient with age. Two different systems are involved in transporting calcium across the membrane in nerve endings or terminals. One system depends on sodium and the other works via a membrane-bound enzyme complex called magnesium-ATPase. Both systems require cellular energy and need calcium to

initiate transport activity. Dr. Michaelis has found in aged rats that these systems are compromised in their ability to transport calcium. Previous researchers have found age-related impairment of calcium transport activity in cells outside the central nervous system (CNS). However, Dr. Michaelis is the first to report decreased activity in the membranes of CNS neurons.

It is unknown whether impaired calcium channel functioning is caused by changes in the membrane's lipid environment or by altered transport proteins within it. What scientists do know is that deficits in membrane transport functioning could lead to prolonged, and detrimental, elevation of calcium inside the cell.

Defects can also occur in other calcium-regulating systems. Studies by Dr. Eva Fifkova at the University of Colorado at Boulder suggest calcium may be elevated in the brain cells of older people because of an impaired ability to store excess calcium. Using electron microscopy, she has detected greater amounts of calcium in the cytoplasm or fluid within dendrites (the fine nerve endings where cell-to-cell communication takes place) of aged rats than in those of younger rats. One of the most important sites where calcium is stored is the smooth endoplasmic reticulum (SER), specialized compartments within dendrites. Dr. Fifkova found that the number of these SER compartments decreases with age while the amount of calcium within the cytoplasm increases. This increase occurs in cells in the hippocampus, which could eventually lead to degeneration of dendrites, and ultimately cell death, as occurs in Alzheimer's disease.

Other studies suggest that calcium clearance may be slower with age. Grantee Dr. Dean O. Smith at the University of Wisconsin drew this conclusion from studies of neurotransmitters released at the junction of neurons and muscles in rats. This NIA-supported study was spurred by the knowledge that release of a neurotransmitter requires calcium to be released from the cell and is, therefore, an indication of how much calcium is inside the cell. Because neurotransmitters cannot be measured directly, Dr. Smith used special techniques to record the electrical activity generated by such transmitters. The electrical recordings were prolonged in the older animals, suggesting that an overabundance of calcium is being released from the cells.

Additional evidence that calcium is elevated in aged neurons comes from NIA-supported investigations carried out at Wake Forest University's Bowman Gray School of Medicine in Winston-Salem, North Carolina. After studying nerve impulses in rats for over 10 years, Dr. Philip W. Landfield may have discovered the physical basis of memory impairment. Using hippocampal cells from young and old rats, Dr. Landfield measured the electrical potential of neurons after activation. After sending impulses, nerve cells normally return to a state called "afterhyperpolarization" (AHP), during which time they cannot

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generate another impulse. In aged cells, the AHP time is prolonged. Because AHP depends on calcium, Dr. Landfield and colleagues suspected that excess calcium inside the cell was the culprit. To test this hypothesis, the Wake Forest team exposed the cells to solutions either high or low in calcium. The results confirmed the calcium link, with AHP prolonged only in cells exposed to high levels of calcium.

Dr. Landfield is also studying the effect of the increased level of calcium on the neuron's ability to receive signals known as "potentiation". This ability is impaired in aged rat hippocampal cells. The research team compared a control group of rats to a group fed a diet rich in magnesium which can block calcium activity in cells grown in tissue culture. The animals were then anesthetized, and electrodes were used to measure the cells' electrical activity. Potentiation was enhanced in the group fed magnesium. Of even greater practical importance, behavioral task performance improved dramatically in both young and aged animals.

The evidence from these four studies on defective calcium regulation provide an interesting, albeit still speculative, explanation that may tie together many of the hitherto unrelated pieces of the Alzheimer puzzle.

A plausible reason for the disruption of calcium homeostasis was presented earlier this year at a three-day symposium jointly sponsored by NIA and several pharmaceutical firms with an interest in neuronal plasticity. (Plasticity is the cell's ability to sprout new dendrites.) Dr. Robert M. Sapolsky from Stanford University in California discussed his research on the effect of glucocorticoids in the brain of aged rats. Glucocorticoids or GCs are a type of stress hormone that are produced in the adrenal gland and that circulate in the blood. Prolonged exposure to elevated levels of GCs disrupts a cell's ability to use glucose, which provides energy to cells. This energy depletion can in turn affect calcium activity. Dr. Sapolsky explains that cells in the hippocampus have a large number of GC receptors, which makes them particularly susceptible to damage from prolonged exposure to these steroid hormones. While Dr. Sapolsky found only a 30 percent reduction in glucose transport, he speculates that this may be enough to render a cell vulnerable to injury from a variety of neurotoxins or other environmental insults. The energy disruption seen by Sapolsky is corroborated by evidence of reduced glucose utilization in areas of the brain affected by Alzheimer's disease.

While agreement on the calcium hypothesis is far from unanimous, the idea that there may be a common pathway to the changes seen in aging and dementia is gaining increasing acceptance in scientific circles. Extending research on cellular mechanisms of calcium regulation should yield important answers about the role of this essential element in health and disease.

Growth Factors: Augmenting a Cell's Natural Ability to Repair Itself

At the same time that some scientists are studying the mechanisms of Alzheimer's disease, other scientists are looking for ways to halt or reverse the disease process.

An exciting area of inquiry has opened up in the area of neuroplasticity as it is mediated by nerve growth factor (NGF). NGF is one of a number of growth factors, or specialized proteins, that promote cell growth and repair. Grantee Dr. Fred H. Gage of the University of California, San Diego has successfully transplanted tissue into damaged brains of rats, resulting in increased cell survival. The transplanted tissue was derived from connective tissue cells called fibroblasts which were genetically modified to secrete NGF. The grafts prevented the degeneration of cholinergic neurons, nerve cells that use the neurotransmitter acetylcholine as the principal chemical for cell-to-cell communication. These are the same type of cells as are affected in Alzheimer's disease. Current studies are aimed at replicating this work in non-human primates and at determining if the grafted cells have any long-term effect on memory and functioning in rats. In the meantime, important questions remain concerning the optimal methods for tissue grafting.

Meanwhile, grantees at the Johns Hopkins University Alzheimer's Disease Research Center are evaluating the usefulness of NGF in animal models more closely related to humans. Drs. Vassilis E. Koliatsos and Linda C. Cork are attempting to deliver NGF to the brains of monkeys with impaired cholinergic function to determine the effectiveness of this treatment in restoring cell function and reversing associated memory deficits. These studies pave the way for future therapies that may one day restore the cell's ability to reconstruct neural pathways in the brain damaged by injury or disease.

THA Study Continues

In mid-July, NIA grantee Dr. Kenneth Davis at the Mount Sinai School of Medicine in New York City announced that analysis of early results from a clinical trial of THA in patients suffering from Alzheimer's disease were not clear-cut enough to halt the trial, but were encouraging enough to warrant continuation of the study.

THA--or tetrahydroaminoacridine--is one of several drugs being tested as a possible means to control memory loss in patients with Alzheimer's disease.

The announcement followed examination of data on the first 100 patients by a small executive committee and presentation of the committee's recommendations to the NIA. The 16-site trial, which began in August 1987 and which was designed to test the drug in 300 people, is being coordinated by Mount Sinai in

cooperation with the Warner Lambert Company and the Alzheimer's Association.

The results of the interim analysis of the first 100 patients didn't answer the question of whether the drug would be effective in the general population of Alzheimer patients. As the study approaches its conclusion, perhaps sometime in 1990, the investigators hope to determine the value of THA as a treatment for memory problems in Alzheimer patients.

Compound Enhances Memory in Rats: Clinical Trials Underway

Other investigators are looking for alternate ways to slow or reverse the more serious symptoms of Alzheimer's disease.

A naturally-occurring compound found in many regions of the brain may enhance certain memory functions known to deteriorate with age. NIA grantee Dr. Carol A. Barnes at the University of Colorado at Boulder has reported some improvement in memory of aged rats after administering acetyl-l-carnitine, a derivative of carnitine (also known as Alcar). Carnitine mimics the action of acetylcholine, a chemical that is necessary for nerve cell communication and that is depleted in Alzheimer's disease. The study was a cooperative effort including the NIA Gerontology Research Center and the Johns Hopkins University, both located in Baltimore, Maryland.

Dr. Barnes and her associates noted improvement in the rats' performance on tasks that involved long-term memory processes. Autopsy studies indicated that chronic administration of Alcar reduced the loss of cells in the hippocampus. By measuring electrical activity of brain cells in rodents, Dr. Barnes has shown that there is an age-related decay in spatial memory, the ability to remember physical orientation of a person or object. These are the types of tasks in which the Alcar-treated rats improved, leading to the notion that the compound may improve thinking, learning, and memory by preserving connections at the junctures between nerve cells.

Because of the improvement seen in rats and because of the compound's apparent lack of toxicity, clinical trials of Alcar are now being carried out in the United States and several other countries to determine the drug's ability to alleviate the symptoms of Alzheimer's disease. In this country, a limited number of patients will be treated with the compound in a four-site study sponsored by an Italian pharmaceutical company and directed by Dr. Richard Mayeux at Columbia University's College of Physicians and Surgeons. The outcome of this study will help determine the future utility of Alcar for treating Alzheimer's disease specifically, and for reducing age-related memory loss in general.

New Technique May Improve Efficiency of Drug Trials

Scientists conducting clinical trials with Alzheimer patients are plagued by several problems. First, there is no definitive diagnostic test for Alzheimer's disease. Invariably, then, the research population includes people with conditions that mimic the disease. Second, the symptoms and course of Alzheimer's disease vary considerably among patients. This means that large numbers of patients are needed in drug trials to determine whether or not the drug has any effect. To address this latter problem, NIA intramural scientist Dr. James Haxby has developed a method to predict an individual patient's rate of decline.

After studying patients for 3 to 5 years, Dr. Haxby noticed that some go through an early plateau phase that may last as long as three and one-half years. The only apparent symptom in these mildly demented patients is memory loss; other intellectual abilities remain unchanged. Using a global test of intelligence known as the WAIS-IQ test, Dr. Haxby found a remarkably steady rate of decline following the initial plateau phase of the disease. Thereafter, patients begin to have problems processing complex information, understanding abstract reasoning, and planning. The test also shows a steady rate of decline in those patients with more advanced symptoms. It seems that while different patients can have markedly different rates of decline, the rate of decline for an individual varies little from year to year. Consequently, a patient's future performance can be predicted based on an established pattern.

Dr. Haxby's approach might be valuable not only in evaluating the effectiveness of experimental therapies, but also in helping physicians and caregivers plan for the care and treatment of each Alzheimer patient by providing more accurate prognostic information.

Helping Families Manage Alzheimer's Patients at Home

Most Alzheimer patients live at home where they receive care and assistance from friends and relatives. As the disease progresses, a patient's need for continuous care places a great deal of stress on the caregiver. In order to determine how best to assist families and reduce the burden of care, NIA-supported scientists are studying the most important causes of stress among caregivers.

While most research in this area focuses on the caregiver-patient relationship, one investigator has shifted his attention to stress-inducing factors beyond the caregiving situation. Dr. David A. Chiriboga and co-workers at the University of Texas Medical Branch in Galveston have compared various stressors that affect caregiver well-being. They find that what happens at work, having a problem child in the household, and other social or family conflict often contribute more to caregiver stress than

the day-to-day responsibilities of providing care.

These findings suggest that any test of the burden of care needs to consider the broad context of life in the family and at work. They also indicate that any program designed to reduce the stress of caregiving needs to involve strategies tailored to individual circumstances.

At the University of Washington in Seattle, Dr. Peter P. Vitaliano and colleagues are examining the health impact of caregiver personality and coping styles on Alzheimer patients as well as on caregivers themselves. The investigators looked at the relationship between patients and their caregivers over an 18-month period and found an association between caregivers who express negative emotions and caregiver health.

Using psychological tests and personal interviews, the Washington team found that caregiving spouses who express high levels of emotion--prone to criticize patients, to express hostility toward them, or to become overly involved with them--tend to perceive that their burden is greater than caregivers who are not so prone. This perception of increased burden was especially evident in caregivers of patients least able to care for themselves. According to Dr. Vitaliano, Alzheimer patients with overly critical caregivers may function below their capabilities, which may further exacerbate the caregiver's heightened emotional response.

Dr. Vitaliano also found that this pattern of negative behavior by the caregiver and poor patient functioning was associated with a history of poor health in the caregiving spouse. Specifically, he found that spouses who expressed high levels of emotion were almost three times more likely to have a history of these disorders than spouses with low levels of expressed emotion.

The researchers believe strongly that anger is a major risk factor for distress in caregivers. Therefore, they advise health professionals to be alert to signs of anger in caregivers and consider referring them to support groups or individual therapy to help them cope with the frustrations of their responsibilities.

National Institute of Neurological Disorders and Stroke

As the principal supporter of neurological research in the United States, the National Institute of Neurological Disorders and Stroke (NINDS) is committed to the study of the brain in Alzheimer's disease. NINDS-supported scientists are pursuing basic studies of brain abnormalities associated with this illness, and clinicians are working with patients to improve methods of predicting and diagnosing the disease.

Studying the Brain

In Alzheimer's disease, cholinergic neurons in the basal forebrain frequently undergo selective degeneration. In studying adult rats with experimental brain lesions, NINDS grantee Dr. Franz Hefti of the University of Southern California in Los Angeles has observed that long term treatment with nerve growth factor prevents loss of cholinergic cells. The treatments were equally effective in young and old rats. While various growth factors can promote cell function, NGF has the benefit of acting selectively on the relevant cholinergic cells.

Meanwhile, NINDS-supported scientists at The Johns Hopkins University School of Medicine have been accumulating evidence that aging monkeys experience the same kind of biological and behavioral deterioration as humans. The nonhuman primates therefore may provide a model for studying the progression and treatment of Alzheimer's disease.

The team, led by Dr. Donald Price, found that as macaques lose their ability to remember, they develop neuritic plaques similar to those often found in aging humans. Dr. Price further found tangled nerve fibers in the brain of a monkey that had performed poorly on various tests. This is the first time that these tangles, a hallmark of Alzheimer's, were found in monkeys.

These studies have suggested one possible order in which Alzheimer's brain abnormalities evolve. In these investigations, fiber abnormalities appeared to develop first, leading to abnormal neurons and finally to the deposition of amyloid protein in plaques.

Another NINDS grantee at Johns Hopkins, Dr. Joseph Coyle, has been studying the mechanisms that regulate production of acetylcholine. Low levels of this brain chemical have been linked to memory loss, learning difficulties, and other cognitive impairments typical of Alzheimer's disease. Dr. Coyle found that the drug galanthamine, which inhibits an enzyme that breaks down acetylcholine, improves the ability of mice to remember how to solve a maze. This suggests that galanthamine might help reverse cognitive deficits.

Predicting and Diagnosing Disease

A team of NINDS grantees, led by Dr. Miriam Aronson at Albert Einstein College of Medicine of Yeshiva University in New York City, has found that memory testing is a promising tool for predicting the development of dementia. By analyzing memory tests given 1-1/2 years before diagnosis, the scientists can improve prediction of the condition's onset over the present rates of prediction.

The Aronson study, which has followed 488 people over the age of 75 for 9 years, also has substantiated preliminary evidence that women are more susceptible than men to developing dementia, particularly the progressive type associated with Alzheimer's disease. It also appears that women with a history of actual or silent (detected only by electrocardiogram) myocardial infarction are especially vulnerable.

Other scientists have been looking for changes in cerebral physiology that may signify early Alzheimer's disease as distinct from other forms of dementia. Using a brain imaging technique called positron emission tomography (PET), investigators make images of the brain after a subject has been injected with a tracer chemical, which acts as a radioactive tag for glucose. The images reveal rates of glucose metabolism in different areas of the brain.

A team of NINDS grantees, led by Dr. David Kuhl at the NIA-supported University of Michigan Alzheimer's Disease Research Center in Ann Arbor, previously had found that metabolic rates are distinctively abnormal in people with probable Alzheimer's disease as well as in symptomatic patients who do not yet meet diagnostic criteria for the disease. More recently, the team has found an exceptional tracer chemical, TRB, for determining the nature and distribution of brain acetylcholine receptors. TRB, which the scientists plan to use in human studies, is easier to make than previous tracers and achieves better distribution in the brain.

National Institute of Allergy and Infectious Diseases

Although there is little evidence that an infectious agent causes Alzheimer's disease, the National Institute of Allergy and Infectious Diseases (NIAID) is interested in it because there are several similarities between it and known viral diseases.

Clue to How Modified Protein Might Evolve in Alzheimer's Disease

As noted in the NIA section of this report, the brain lesions that characterize Alzheimer's disease are made up of a modified form of amyloid protein. How this protein becomes modified may be important for understanding how the disease develops.

NIAID grantee Dr. Timothy Wong and colleagues at the University of Washington in Seattle are studying a rare brain disorder, subacute sclerosing panencephalitis (SSPE), linked to the measles virus. Their work may provide clues to how modified proteins could evolve in the central nervous system.

In studying strains of measles virus isolated from brains of SSPE patients, the scientists have found that part of the genetic material of the measles virus is highly susceptible to specific mutations when grown in brain cells as compared with cells from other parts of the body. Once the changes are induced, they are passed on to new virus particles, which then spread slowly to other cells, perpetuating the modification. Brain cells infected with the modified virus tend to accumulate proteins of the modified virus, rather than release fully formed viruses.

Specific mutations in the genetic material coding for one protein of the measles virus appear to produce the chronic measles virus infection of the brain that characterizes SSPE. If similar, non-random changes can occur to cellular materials, this could explain how modified cellular proteins could be produced that might accumulate in the host brain. This poses an intriguing question, whether modified proteins involved in degenerative central nervous system diseases, such as the amyloid protein in Alzheimer's disease, might be produced by this mechanism.

Laboratory System Developed to Help Understand Scrapie

Many studies indicate that a modified form of a normal brain protein, prion protein (PrP), is associated with scrapie, a neurodegenerative viral disease of sheep and goats. In scrapie, a fibrous protein accumulates in plaques and tangles of nerves in the brain, creating lesions similar to the protein-laden plaques and tangles seen in the brains of Alzheimer patients.

Last year at NIAID's Rocky Mountain Laboratories in Hamilton, Montana, intramural scientists Drs. Bruce Chesebro, Byron Caughey, and Richard Race developed a system to study PrP and the scrapie agent. The system comprises scrapie-infected cells growing in mouse brain tumor cell clones.

Now able to carry out experiments more efficiently, the investigators recently used the new system to determine how PrP is normally made and whether scrapie infection alters this process in any way. They found no evidence that scrapie infection modifies PrP biosynthesis in these animal cells.

Some scientists believe that modified PrP is a necessary component of the infectious scrapie agent, but these experiments did not verify this hypothesis. The modified form of PrP may instead arise as a byproduct of the disease process in a way that scientists cannot yet duplicate in the laboratory. The intramural scientists have now begun to analyze the process by which PrP is made to determine what else might influence the modification of PrP.

Division of Research Resources

The Division of Research Resources (DRR) supports and conducts research into Alzheimer's disease at research facilities across the United States. The DRR Biomedical Research Support (BRS) Program provides a pool of flexible funds to institutions heavily engaged in Public Health Service-funded research aimed at meeting particular research-related needs not usually covered by other grants. This year the work of Dr. Dennis Selkoe, highlighted in the NIA section of this report, utilized equipment provided by the BRS Program.

Other studies are looking at computed tomography (CT) as a means of identifying Alzheimer patients. According to Dr. Godfrey Pearlson at The Johns Hopkins University General Clinical Research Center (GCRC), which is supported by DRR, CT scans indicate significant decreases in the amount of brain tissue in these patients over the course of just one year.

GCRC's provide the research infrastructure for multidisciplinary studies on both children and adults. Specifically, they provide patient research facilities, computerized data management and analysis, as well as support for research nurses, dieticians, biostatisticians, and specialized laboratories for the translation of basic and clinical research into medical practice.

Dr. Pearlson and other GCRC grantees examined 24 patients with early probable Alzheimer's disease and 20 age-matched healthy people. The patients were scanned at yearly intervals; the normal individuals were rescanned after 4 years. Regional volumes of cerebrospinal fluid (CSF)--the fluid that is secreted by specialized cells into the brain ventricles (spaces in the largest part of the brain)--were calculated. The grantees reasoned that the greater the volume of CSF, the larger the ventricles. If the patients do not have any other conditions, then the ventricles can expand only with the atrophy of brain tissue. Therefore, expanding volumes of CSF indicate increasing atrophy of brain tissue.

Dr. Pearlson found that CSF volumes were significantly larger after just one year in patients with Alzheimer's disease. So significant was the atrophy, in fact, that these patients, as a group, showed a greater increase in CSF volumes after 1 year than was seen after 4 years in the healthy group. Future studies are planned to determine if this technique is effective in rapidly identifying early cases of Alzheimer's disease.

National Center for Nursing Research

The National Center for Nursing Research (NCNR) supports research on Alzheimer's disease that focuses on developing and testing nursing techniques to improve home care as well as institutional care of Alzheimer patients. Studies also are aimed at developing better ways to educate and assist family caregivers.

Scientists Look for Successful Behavior Management Methods to Facilitate Home Care for Alzheimer Patients

Caring for Alzheimer patients can be difficult because patients are often confused and anxious and display inappropriate behavior, such as wandering, ignoring personal hygiene or being combative. Family members who care for these patients at home often report high stress, depression, poor health and low life satisfaction.

Providing family members with information about successful home care methods can help them cope better with a routine that can be complicated and exhausting. NCNR grantee Dr. Mary Stewart-Dedmon of the University of Iowa College of Nursing in Iowa City is interviewing family members who provide home care for Alzheimer patients. She is collecting information from 40 families about the most frequent memory and behavior problems they observe in patients, how the families manage these behaviors, and the usefulness of various behavior management techniques. The investigators plan to incorporate information about successful care methods in an Alzheimer's education model for health teams to use in helping families manage the needs and demands of people with Alzheimer's disease.

Researchers Evaluate Special Long-Term Care Unit for Alzheimer Patients

The progressive mental and functional impairments of Alzheimer patients pose many difficult problems for nursing care and management in long-term care facilities. Although long-term care units especially designed and equipped to treat patients with Alzheimer's disease do exist, there have been no systematic studies of their effectiveness.

With grant support from NCNR and NIA, Dr. Meridean L. Maas of the University of Iowa College of Nursing is assessing the effects of a special unit for the care of Alzheimer patients on patient functioning, family attitudes toward care, and staff morale, as well as on costs of care. The unit, located at the Iowa Veterans Home and administered by nurses, is designed to be environmentally safe, to have built-in cues to improve patient orientation and help avoid confusion, and to facilitate health care workers' ease of care.

Dr. Maas and her colleagues are comparing the efficacy of the special unit to that of traditional units that integrate Alzheimer patients with other residents. The investigators are comparing rates of decline in patients' mental and functional abilities, degrees of agitation, use of medication, safety and extent of participation in social and recreational activities. They also are measuring family perceptions of patient care. In addition, the researchers are looking at the level of knowledge, amount of stress, degree of job satisfaction and rate of absenteeism among staff members.

Determining the usefulness of a special Alzheimer unit can help long-term care administrators, clinical staff, and families of patients plan the most effective and least costly means of care.

Outlook

In 1989, the Department of Health and Human Services took a major step in support of Alzheimer's disease research with the publication of the report of the Advisory Panel on Alzheimer's Disease. The report called for increased funding for biomedical research as well as for research related to services for Alzheimer patients.

In addition, the NIA announced the establishment of three new Alzheimer's Disease Research Centers. This brings the number of such centers to 15 in a nationwide program designed to enhance research and care by establishing a network for collaborative efforts.

Also in 1989, the NIA and the Administration on Aging hosted a series of conferences focusing on issues faced by caregivers of Alzheimer patients. The 14 conferences, held in 9 different states, provided training and information about current practices in caregiving support for families of Alzheimer patients.

In international research, the World Health Organization Special Program for Research on Aging (which is based at the NIH campus so it can draw upon NIA resources and scientific expertise) moved forward in its plans for a comparative population study on age-associated dementias. This year, WHO announced that the project would be coordinated by the Studio Multicentrico Italiano Sulla Demenza in Florence, Italy, with Canada, Chile, Malta, Nigeria, and Spain participating in the study.

New research initiatives for the coming year include increased efforts to direct attention toward developing and testing behavioral, social, and environmental interventions for reducing the burdens of care, and evaluating the utility of special Alzheimer units in day care and long-term care settings.

As we begin 1990, the "Decade of the Brain," it is incumbent upon NIH to aim for a better understanding of the basic nature and causes of Alzheimer's disease and to find a way to diagnose, treat, and care for the 4 million people who suffer from it.

CENTERS FOR DISEASE CONTROL

Alzheimer's Disease and Related Disorders

Dementias are the most common chronic neurological problem, estimated to affect 5-10% of the population over age 65, and are certain to become an increasing burden on the health care system given the rapid aging of the population. Alzheimer's disease (AD), the most common cause of dementia, has been the focus of considerable research in recent years. The understanding of the genetics, pathophysiology, discriminating diagnostic criteria, and possible biological markers of AD has increased in recent years, but knowledge of its epidemiology is scant. Only one study has examined the prevalence of AD anywhere in the United States, and none has looked at incidence.

During 1988-89 CDC developed a cooperative agreement with the South Carolina Registry of Dementing Illness as part of an initial effort to obtain valuable epidemiologic knowledge of dementias. Unfortunately, key staff changes within the South Carolina group resulted in their inability to successfully implement the registry as originally proposed and CDC staff found it necessary to discontinue the project. Nevertheless, this initial effort provided a valuable object lesson in critical aspects of developing dementia surveillance in cooperation with states. During this same period other States have proceeded with development of dementia registries and other surveillance efforts using their own resources.

The surveillance of dementias has a variety of difficulties, primarily those of validity and completeness, due to the lack of simple, operational, diagnostic criteria and incomplete case finding. Incomplete case-finding results from confusion of dementia with natural aging, so that many cases never enter the medical care system; the tendency of many primary care physicians to underdiagnose dementias; and the lack of centralized access to cases, because most persons are diagnosed as outpatients. Nevertheless, public concern about dementias has been great enough to spur several State health departments to attempt surveillance.

Evaluations of these strengths, weaknesses, utility and cost effectiveness of State surveillance programs would come from the comparison of surveillance data to dementia registries, and the review of pathology records, death records, surveys of cognitive function among the elderly, and other sources.

To assist States with addressing the problems associated with dementia surveillance and development of public health program activities to assist Alzheimer's victims and their families, the following activities will be conducted:

- A group with expertise in neurology, epidemiology, and public health practice will be established to provide expert consultation and oversight regarding research activities as well as advise on future directions for dementia programs.

- A descriptive study of the impact of dementias on the family will be conducted. The study will focus on the effects on family members, particularly the caregiver, of caring for a dementia patient.

- An evaluation of State dementia registries will be conducted in 1990.

CENTERS FOR DISEASE CONTROL

National Center for Health Statistics

ALZHEIMER'S DISEASE

According to the 1987 National Hospital Discharge Survey, an estimated 119,000 patients were discharged from short-stay hospitals in the United States with a diagnosis of Alzheimer's disease on the medical record. In almost all cases, this diagnosis was a secondary diagnosis; in less than 10,000 cases was Alzheimer's disease the principal diagnosis listed on the medical record.

The Supplement on Aging to the 1984 National Health Interview Survey included Alzheimer's disease on the condition list, and the data from this supplement are now available on public use data tapes. However, the small number of cases suggest that there is underreporting of this condition.

Numbers of deaths attributed on the death certificate to Alzheimer's disease have increased markedly in recent years according to data from the National Vital Statistics System. In 1979, a total of 857 deaths due to this cause were reported in mortality data from NCHS. By 1987, the number had increased to 11,311; over 13 times the number in 1979. This condition was mentioned as contributing to, but not as the underlying cause, for an additional 14,639 deaths in 1987.

ALCOHOL, DRUG ABUSE AND MENTAL HEALTH ADMINISTRATION

National Institute of Mental Health

ALZHEIMER'S DISEASE

On July 25, 1989, President Bush signed a joint resolution of Congress and declared the 1990's to be the Decade of the Brain. The National Institute of Mental Health (NIMH) will be heavily involved in this over-arching initiative in basic and clinical neuroscience and in brain-behavior relationships and disorders. During the Decade of the Brain, a major focus of the Institute will be Alzheimer's disease (AD).

In AD, a progressive destruction of brain cells results in memory loss and impairment of thinking and behavior. It is estimated that over 3 million Americans presently suffer from Alzheimer's disease or related dementias.

The impact of AD on patient, family and society is severe as evidenced by patient dysfunction, family burden and high societal costs. The cost of caring for individuals with AD and related dementias has been conservatively estimated to be $38 billion to $42 billion per year for direct costs alone. The need for appropriate services and high-quality care for AD will grow, especially since effective methods of prevention and cure are unknown at the present time and because the elderly--the group most at risk for AD--continue to increase in number at a high rate.

With the prevalence of this debilitating neuro-degenerative disorder increasing rapidly and the public health burden growing increasingly more serious, research on AD must be approached on a variety of fronts. NIMH is very committed to promoting and supporting research on multiple aspects of AD as a clinical disorder, including work in the neurosciences, the behavioral sciences, and services research. The areas studied range from investigations of potential etiological factors to evaluations and cost-effectiveness studies of promising models of delivering services to patients with AD and their families.

Research: Etiology, Pathogenesis and Diagnosis

Although the cause of AD has not yet been determined, rapid advances are being made in clarifying multiple aspects of the etiology of this disease particularly in terms of its molecular genetics. These advances may lead to the discovery of a diagnostic marker for early stages of AD and to clinical interventions to slow or halt the disease.

Studies have shown that the brain of the AD patient loses specific nerve cells and develops characteristic pathological changes, recognized under the microscope after death. The changes that are the hallmarks of the disease are: cell loss; the neurofibrillary

tangle, an abnormal nerve cell body filled with masses of twisted proteins called paired helical filaments; and the neuritic plaque, a focal collection of degenerating nerve endings surrounding a core of "amyloid" protein. Cell loss, tangles and plaques occur primarily in the brain regions associated with higher cognitive functions (i.e., learning and memory). These areas are the cerebral cortex, the hippocampus, the amygdala, and some deep brain areas, particularly the basal nucleus.

At present, genes are the only causal factor conclusively identified and, thus, provide the only confirmed clue to unraveling the mystery of this disease. One of the most exciting aspects of current research on AD is the attempt to identify the chemical structure, source and pathogenesis of the fibrous proteins that characterize the plaques. This line of inquiry has shown great promise for elucidating genetic mechanisms of the disease and, potentially, for leading to clinical interventions. Evidence supports the conclusion that both the vascular and plaque amyloid of AD have the same principal component, which is a beta-protein. Whether this protein is produced in the brain or in another body organ remains unknown. Studies have revealed that the beta-protein is made up of fragments of a larger protein molecule that normally spans the nerve cell membranes. Since preliminary data indicate that the gene coding for this beta-protein is in all the cells of the body, scientists are asking why it should be selectively expressed in the brains of AD victims. Molecular genetic techniques have been employed to study the origins of amyloid in both familial AD (cases occurring with a significant family history of AD in ancestors) and sporadic AD (cases without such a family history).

Several investigators have located the amyloid protein gene on chromosome 21 adjacent to a region associated with Down's syndrome, a developmental disorder of genetic origin. This common genetic base on chromosome 21 provides a rationale as to why individuals with Down's syndrome who achieve 40 years of age develop Alzheimer-like neuropathologic changes. Other research has provided evidence that a significant excess of Down's syndrome births occur in families identified by of a case of AD.

Additional markers linked to familial AD have also been identified on chromosome 21. Despite initial hopes that the two genes might be more closely linked, the most recent molecular studies have shown that the marker gene for familial AD and the gene for beta amyloid protein are not identical but reside at separate points on chromosome 21.

The molecular genetic findings on familial AD have been based primarily on information pooled from several families showing a large number of AD cases and an autosomal dominant pattern of inheritance, which means that offspring of an AD patient had a 50 percent chance of developing the disease. Additional such families will constitute an important resource for researchers attempting to identify, through molecular genetic approaches, the

gene responsible for AD. Accordingly, NIMH has initiated a multi-center program in which appropriate additicnal families will be sought and tissue banks established to support genetic studies of several major mental disorders. Three centers will focus on AD.

Along the same lines, a previously funded project has been establishing lymphoblastic cell lines on all available members of at least five families which are affected by autopsy-proven diagnoses of AD in a pattern consistent with transmission by an autosomal dominant gene. These cell lines can be used as a permanent source of DNA from each family member and will allow identification and characterization of the DNA sequence critical in AD. This methodology can be extended to additional large Alzheimer's kindreds as they are identified. Although the pace of discovery in molecular genetics has been rapid, the prospective collection of tissue samples should accelerate further the identification of the gene(s) involved in AD. As new technologies become available, they can be applied immediately to these multi-generational samples rather than having to wait for a new generation of patients to develop confirmable AD.

The search for causes has begun to focus on the problem of why nerve cells in particular parts of the brain are selectively vulnerable to death in AD. Several studies have indicated that in old animals, as well as in surgically treated experimental animals, a substance termed nerve growth factor (NGF) and other growth-promoting agents usually act to support the viability and functioning of nerve cells. Many scientists believe that an important reason for selective cell death in AD may be a decline in the supply of growth-promoting (or trophic) factors that normally maintain the functioning of brain cells. Recently, scientists synthesized the first 28 amino acids of the amyloid protein and demonstrated that amyloid has a trophic, or growth-enhancing, effect on nerve cells. Other scientists have found that a larger fragment of the amyloid protein, about the first 50 amino acids, may have toxic effects upon neighboring cells when released from the cells which have been stimulated to overproduce it. It thus appears that plaque formation in AD may represent the attempt of nerve cells to mount a defense against the degenerative process and to compensate for the damage that occurs as the disease progresses. However, events in the early stages of AD, may lead to the production of an abnormal amyloid protein that malfunctions and contributes to the progress of the disease.

Much of the work on neurotrophic factors has focused on cell survival in the hippocampus, an important brain structure involved in the mechanism of memory storage. Animal studies have indicated that specific nerve growth factors can stimulate the growth of new synaptic connections following lesions placed in the hippocampus and, as a result, restore experimentally produced memory loss. Techniques of stimulating the production of these trophic factors, or of using them to support the transplantation of neural tissue, therefore hold great promise for alleviating the symptoms of memory impairment seen in AD.

The nerve cells that are selectively vulnerable in AD produce important neurotransmitter molecules which are lost in the disease process. The best example is the nerve cell group called the cholinergic system, which produces acetylcholine, a neurotransmitter of demonstrated importance in memory processes. Acetylcholine has been shown to be important in the etiology of AD since loss of cholinergic neurons is almost always observed in the brains of patients who have died from this disease.

Using a prototype SPECT (Single Photon Emission Computed Tomography) scanner, NIMH intramural scientists have, for the first time, visualized the location of cholinergic neurotransmitter systems in the living human brain. The scans, which trace the uptake of iodinated QNB (a cholinergic antagonist), reveal the distribution of muscarinic acetylcholine receptors or binding sites on cell surfaces. These binding proteins are part of a messenger chemical system known to be associated with memory loss in Alzheimer's disease. SPECT scan studies reveal major deficiencies in muscarinic acetylcholine receptors in the parietal cortex and other brain regions of Alzheimer's patients.

Additionally, studies on the role of neuropeptides in brain function are increasing knowledge of the mechanisms of neuronal communication and the multiplicity of chemical messengers involved in that process. It is becoming increasingly clear that neuropeptides--small proteins that are secreted by brain cells along with major neurotransmitter chemicals and that fine tune the activity of the latter--play a central role not only in normal brain physiology, but also in pathophysiologic states such as AD. Interaction between neurotransmitters and neuropeptides is common in the brain and may hold a key to understanding underlying neural mechanisms of AD and to developing new, more selective classes of drugs for treating AD.

One group of scientists, for example, is finding that neuropeptide modulators of brain cholinergic neuronal activity can affect experimentally-induced memory impairment in animals and humans. The research team employs animal models to test potential new drugs that affect classical neurotransmitter function by targeting particular neuropeptide systems.

The studies focus on galanin, a peptide that coexists with acetylcholine in neurons that mediate memory processing. Using an animal model of Alzheimer's disease, the research team has found that while acetylcholine improves the maze-running performance of rats whose memory systems are chemically impaired, this beneficial effect of acetylcholine can be inhibited by galanin. This work suggests that a drug that antagonizes galanin might help Alzheimer's patients whose acetylcholine systems are similarly impaired.

Other researchers are studying somatostatins, peptides which are particularly interesting because they have significant effects on

both reducing cellular responses to excitatory amino acids (EAAs) and potentiating cholinergic effects [there is strong evidence that a major source of damage to memory systems is the toxic effects of excitatory amino acids on structures such as the hippocampus, and acetylcholine (cholinergic neurotransmitter) has long been thought to be a key transmitter in memory formation and is markedly reduced in Alzheimer's disease]. One scientist is using recently developed methods for recording the electrical currents generated by single brain cells and is determining how these electrical phenomena change when the cells are exposed to different pharmacological agents. In addition, the researcher will use immunohistochemical techniques to make somatostatin-containing cells visible under the microscope so that their anatomy can be investigated. These studies will provide a picture of how somatostatin influences cellular responses to other brain chemicals and would be an important step toward designing drugs that might prevent memory loss.

The diagnosis of AD remains a major challenge for scientists today. A definite diagnosis can be accomplished only by examining the brain at autopsy. The search continues for peripheral physiological markers that might be used in live patients in a diagnostic test for AD.

Scientists have extended and clarified the initial findings of a blood platelet abnormality in AD patients, namely, increased membrane fluidity, hypothesized to be a product of the AD gene. There is now evidence that this membrane abnormality identifies a subgroup of patients with distinct clinical features--including an earlier symptomatic onset, a more rapidly progressive decline, and greater likelihood of a family history of dementia--and that it appears to be a stable, familial trait vertically transmitted in families through inheritance of a highly penetrant autosomal gene. Following the recent discovery that the genetic locus for this trait may reside on the long-arm of chromosome 21, a linkage analysis study is now being undertaken to determine definitively whether the trait is located in this region of chromosome 21 or closer to a region associated with the development of Down's syndrome and whether it is distinct from the genes for familial AD and the amyloid precursor protein. Further investigations are needed to determine the sensitivity and specificity of platelet membrane fluidity relative to AD before its practical usefulness as a diagnostic marker for AD can be determined.

Another line of research has discovered an abnormal protein (A-68) in the brains of AD patients. The largest concentrations of this protein are in the vital memory areas. Recently, A-68 was reported to be present in cerebrospinal fluid (CSF) which could facilitate its value in diagnostic testing.

Other researchers, studying somatostatins, found that: 1) CSF somatostatin was significantly decreased in a large group of Alzheimer's patients compared with the age-matched controls; 2) values of CSF somatostatin in Alzheimer's patients were

significantly lower than in elderly depressives, but values in the latter group were lower than those found in controls; and 3) in Alzheimer's patients, there was a correlation between levels of CSF somatostatin and ratings of depression.

Research has also been directed toward identifying electrophysiological (EEG) and radiological indicators that may have diagnostic utility in AD. Studies of EEG sleep data in AD patients by several researchers have shown great promise of demonstrating sleep patterns that differentiate early Alzheimer's disease from depressive disorder in elderly patients. One study found that by looking for a particular EEG measure, and also noting how wakeful each person was, investigators could correctly classify 85 percent of the individuals in a mixed group of people that included some who had aged normally and some who had mild dementia.

In another project, investigators were able to use sleep patterns and response to sleep deprivation to successfully predict which patients would show worsening dementia and which would develop a serious depressive illness with symptoms resembling those of dementia.

Other investigators have found that computerized analysis of the EEG signals can be used to distinguish patients with AD from those with dementia caused by multiple strokes (multi-infarct dementia). More than 90 percent of the people studied could be correctly classified by this method.

Using various brain imaging techniques, investigators have found that AD appears to involve changes in the inner portions of the brain rather than in the outside (cortical) regions where the major changes of normal aging take place. In particular, positron emission tomography (PET) scanning has shown metabolic changes deep in the brain in Alzheimer's patients. Also, investigations using computerized tomography (CT) and neuromagnetic resonance (NMR) imaging have found twice the incidence of leukoencephalopathy (decreased white matter density) in AD patients compared with controls. These changes are especially pronounced in the brain's frontal lobe. Their significance is still being investigated.

NIMH researchers have also found that AD patients reveal increased sensitivity to brief challenges with the anticholinergic agent scopolamine, relative not only to age-matched normal controls but also relative to elderly depressives. These results suggest that such testing may have diagnostic utility, particularly in differentiating depression or "pseudodementia" from AD. Ongoing studies to test this hypothesis are using at-risk family members and other non-AD populations.

Treatment

Interventions to Aid Patients

Many scientists are searching for drugs that will safely and effectively slow or reverse the symptoms of AD. It has been well established that the brains of AD patients show marked reductions in the levels of certain neurotransmitter substances, such as acetylcholine, which are essential to normal memory function. The most widely tested agents have been drugs that block an enzyme, cholinesterase, that normally breaks down acetylcholine in the brain. Several investigators have reported that a proportion of AD patients treated with one such drug, physostigmine, have shown mild, transient improvements in memory at the early stages of the disease, though others have conflicting findings. A major difficulty has concerned the limited usefulness of the drug due to its short duration of action (physostigmine has a plasma half-life of only 30 minutes).

However, in an open trial with AD patients, investigators have found that a long-acting anticholinesterase drug, metrifonate, achieved up to 80 percent inhibition of cholinesterase without causing interfering side effects, could be administered safely for up to 5 months, and may improve cognitive performance in AD patients as judged both by clinical reports from patients and their families and by psychological evaluations. The findings suggest that this drug may be highly useful in further research and may enable definitive tests of the hypothesis that depletion of the neurotransmitter acetylcholine is the central neurobiological pathway leading to the cognitive deficits seen in AD. The same investigators are now being funded to conduct a double-blind clinical trial of metrifonate in AD.

Certain neuropeptides, the endogenous opioids, also appear to play an important role in the memory processes, and their interaction with cholinergic systems may be important in the learning/memory capacity of both young and aged animals. Studies have found that administration of drugs that promote (agonist) and retard (antagonist) the action of natural brain opioids can affect memory formation in experimental animals. Scientists have found that naloxone, an opiate antagonist, enhances retention of memory. This observation, along with that of elevated opioid peptide levels in the aged rat hippocampus, holds promise for the possible pharmacological manipulation of this system by specific drugs which might alleviate memory loss in affected humans.

Preliminary studies are finding that the neuropeptide thyrotropin releasing hormone (TRH) can reverse memory impairments experimentally induced by scopolamine, a drug that temporarily blocks acetylcholine activity. To produce these cognitive effects, investigators give higher than usual doses of TRH to maximize penetration of the blood-brain barrier. Studies testing TRH as a potential treatment in AD are in progress.

Other investigators are simultaneously using multiple classes of drugs that affect different brain systems to determine whether they produce synergistic effects in AD patients. In the first NIMH trial of such a combination treatment, intramural researchers are administering the anticholinesterase inhibitor, physostigmine with l-deprenyl, an antidepressant that produced mood and behavioral improvements in earlier studies.

Another pharmacological approach involves a series of studies with the serotonergic agent, m-chlorophenylpiperazine (m-CPP). Because the serotonin (5-HT) system is severely impaired in Alzheimer's disease, there is potential therapeutic benefit from serotonergically active compounds. Initial findings suggest that m-CPP is safely tolerated and that Alzheimer patients demonstrate increased behavioral but not neuroendocrine sensitivity to challenge with this drug. The next studies include chronic treatment with m-CPP and other serotonergic agents.

Scientists have also found that levels of tetrahydrobiopterin (BH4) are altered in Alzheimer's patients. An earlier finding, that it is only the subgroup of patients with movement disorders who have low CSF levels of BH4, has been extended by showing that those patients with myoclonus (shock-like contractions of the muscles) also show the BH4 deficit. These findings are essential in providing a criterion for the selection of the most suitable Alzheimer patients who might benefit from BH4 administration. Clinical follow-up is under way.

Studies of DHEA (dydroepiandrosterone) levels in patients with Alzheimer's disease also continue. Investigators have found that DHEA levels are lowered in patients with Alzheimer's compared to age-matched controls. Observations that high levels of the hormone DHEA may provide protection against viral illness have led to the initiation of clinical trials of the hormone in Alzheimer's disease patients to determine whether the administration of DHEA has a beneficial effect.

Finally, researchers continue to develop new rating scales to assess elderly patients. During the past year, the Dementia Mood Assessment Scale (DMAS) continued to be used to measure depression in Alzheimer's disease patients and two new rating instruments were also created. The first, a scale to measure the activities of daily living, called the Daily Activities Questionnaire (DAQ), allows quantitative measurement of individual functioning over time. The second, a Clock Drawing Task, focuses on the mostly nonverbal visual-spatial skills of individual Alzheimer patients compared to controls. Both instruments are designed for research purposes but also have immediate clinical applications and will be helpful in testing diagnostic and prognostic accuracy in Alzheimer patients when used longitudinally.

Interventions for Families and Caregivers

Substantial efforts are being directed toward addressing the problems experienced by the families of AD patients, including interventions designed to alleviate the stress and risks for disease that characterize family caregivers. In studying the psychosocial needs of caregivers for AD patients, researchers found that 33 percent had a major affective disorder, that 21 percent met criteria for dysthymic disorder, and that 50 percent rated high on two out of three of the symptoms of dysphoria, anger and anxiety. These findings are helping to direct the development of therapeutic interventions for caregivers which are tailored specifically to fit their target symptoms.

For the first time, there is scientific evidence that family members may show negative changes in their immune systems as a result of the stress of care-giving. It has been previously recognized that, in stressful chronic diseases of the elderly such as AD, care-giving family members may be vulnerable to increased physical symptoms and illness, as well as psychiatric morbidity, with potential long-term health consequences. Several currently funded studies are investigating the chronic impact of care-giving on neuroendocrine and immune functioning and exploring whether these factors may predict which individuals will develop an illness under the stress of care-giving. Preliminary findings in one such project indicated that the family caregivers of AD patients not only often suffered suppression of their immune systems but that the impairment of their immune functioning continued to worsen over a one-year follow-up period in contrast to nonsignificant changes in control subjects. Furthermore, caregivers whose AD patients had died or moved to an institution showed improvements in their symptoms of depression but immunological decline continued over this period, despite the psychological improvement. These findings may be ground-breaking in indicating a neuro-psycho-immunological mechanism whereby health changes in caregivers may take place, and in raising questions about long-term physiological alterations in caregivers following years of chronic stress.

Services Research and Systems of Care

Services research plays an important role in advancing the development of validated clinical and service delivery approaches to address the immediate needs of AD patients and their families. When service delivery programs are evaluated within a research framework, the likelihood of developing reliable and generalizable models increases. Today, improved coordination of research initiatives and the burgeoning of the scientific literature on AD have enhanced the capacity of the field to conduct new and improved studies of services.

Surveys conducted through a national reporting program have generated new data on the role of the mental health system in providing care for dementia victims. In 1986, approximately 26,000 persons were admitted to mental health inpatient, outpatient, and partial care programs with a principal diagnosis of primary degenerative dementia. More than 70 percent of these persons were

admitted for inpatient care. State and county mental hospitals and non-Federal general hospitals with separate psychiatric services were frequent sites of inpatient care, while multiservice mental health organizations and non-Federal general hospitals were frequent sites of outpatient care.

One currently funded service demonstration project is evaluating the effectiveness of providing trained respite care workers to care-giving families of AD patients in terms of both improvements in the families' quality of life and reductions in the patients' institutionalization rates. Another project is evaluating a model program for elderly persons disabled with AD or other chronic mental disease which encompasses individual assessment and treatment planning, case management, and supported referral. Patients receiving the program are being compared with controls in terms of their functioning, maintenance of residence in natural community settings, services utilization, mortality and morbidity rates, and quality of life.

NIMH has reissued and continues to support a longstanding grant announcement for "Research on Family Stress and the Care of Alzheimer's Disease Victims" which incorporates requests for grant applications for services research on treatment and family support. The Institute has also issued two other program announcements requesting research grant applications on services for severely mentally ill persons, including patients with AD, one of which deals with the cost and reimbursement of mental health services for AD victims.

NIMH also continues to fund a number of projects conducting research on mental illness, including dementias, in nursing homes. One such project is currently analyzing data on the prevalence and severity of mental impairments and disordered behaviors among more than 189,000 nursing home residents from 1,965 facilities in three States. The researchers are also studying various institutional responses to disordered behaviors such as physical restraints, psychotropic drugs, and alternative management strategies. The goal of the study is to assist in the development of improved strategies of care for mentally ill and cognitively impaired elderly residents of nursing homes.

In support of its services research initiatives on AD, NIMH published a book, "Alzheimer's Disease Treatment and Family Stress: Directions for Research," in which leading researchers discuss the current status of research, substantive and methodological issues, and the future research agenda relative to such topics as the family in AD, care-giver stress, treatment and management of AD patients, and mental health services for AD victims and their families. The Institute also will hold several workshops directed toward defining and fostering new directions in services research on AD.

Areas of program development in services research relating to AD that are expected to expand at NIMH include proposed initiatives

to stimulate more research on: 1) approaches for management of the behavioral and psychiatric symptoms of AD patients, and 2) research directed toward developing models of family care and service delivery for this disorder.

Council and Task Force on Alzheimer's Disease

NIMH currently provides the Deputy Executive Secretary and staff support functions for the Department of Health and Human Services Council on Alzheimer's Disease and the Advisory Panel on Alzheimer's Disease, both of which were established by P.L. 99-660. The Council is composed of Federal employees, whereas the Panel is a non-Federal advisory body appointed by the Office of Technology Assessment.

Representation on the Council includes NIMH, three Institutes and the National Center for Nursing Research of NIH, the Veterans Administration, the National Center on Health Services Research and Health Care Technology Assessment, the National Center for Nursing Research, the Health Care Financing Administration, the Health Resources and Services Administration, the Administration on Aging, and others. Coordination of basic research on the brain and behavior, epidemiology, diagnosis, treatment, costs, and financing is being accomplished. An annual report to Congress details progress in basic and clinical research on AD.

The Advisory Panel recently published the first of four Congressionally mandated reports in which it set forth its recommendations for legislative and administrative actions to improve services for patients with AD and related dementias and their families. It also set forth recommendations on how to provide for promising biomedical research on this disease.

As the Decade of the Brain continues, NIMH will continue to place emphasis on Alzheimer's disease in an effort to answer many of the puzzling questions surrounding the disease and to determine the best treatments and services possible.

HEALTH CARE FINANCING ADMINISTRATION

Alzheimer's Disease and Related Dementias

Nature/Magnitude of the Problem

A patient with Alzheimer's disease (AD) or a related dementia generally requires a full range of medical and personal care services during the course of his/her illness, including hospital, community and home health services, and institutional long term care. It is estimated that more than half (55 percent) of patients in long term care facilities have AD or a related dementia. Nonetheless, it appears that a greater number of persons with dementia reside at home or in the community than in institutions. According to a study funded by the national Institute on Aging, the total costs, including the direct costs of providing services and indirect costs, were roughly estimated to be $8 billion in 1983. A major goal of all services has been to keep the patient at home or in the community, if feasible.

An improved understanding of different approaches to better coordinating health, social, and personal care services for dementia patients and their families--with determination of associated costs--has been another services research challenge. The cost of providing needed health, social, and personal care services for these individuals and their families varies dramatically according to the severity and length of time of the patient's illness, among a number of other factors. Two problems in determining total costs for these individuals and their families are that (1) some of the major third party payers of care (i.e., Medicaid and private health insurers) do not routinely categorize their cost data according to patient diagnosis and (2) it is difficult to obtain data about how much is being spent by families and the community in providing needed services to the individuals and their families. At this time, no major studies have been conducted that can provide reliable and accurate information on total (or even average) costs for these individuals and their families.

Medicare

Medicare coverage is determined by the nature of the services required and not by the specific diagnosis of the patient. Therefore, dementia patients are covered for Medicare benefits no differently than other elderly patients requiring medical services. The following is a breakout of dollars reimbursed by Medicare to institutions providing care to patients with AD or a related dementia in 1985: $574 million to hospitals and $11 million to SNFs. In addition, Medicare paid approximately $175 million to physicians and $1.5 million to HHAs providing services to these patients.

Medicaid

Coverage under Medicaid is limited to low-income individuals and families. Only 8 percent of the elderly are covered under Medicaid. However, it is estimated that between 15 and 20 percent of individuals with dementia are covered under Medicaid. Once the individual with AD or a related dementia becomes eligible for Medicaid, he or she is covered under the program for a much wider array of health, medical and personal care, and long term care services than the patient covered only under Medicare. In addition to covering the services such as hospital, SNF, ICF, and physician services, States are given the flexibility of covering under the Medicaid program home and community provided personal care services, private duty nursing, physical therapy, clinic services, and drug costs.

Private Health Insurance Programs

Significant changes having been occurring in the private long term care insurance market. Nationwide the number of individual long term care policies has doubled in the last 2 years to an estimated 500,000, provided by over 70 companies. Early private long term care insurance products (1986) were limited by the fact that they tended to cover acute and subacute care services (i.e., SNF services) but to exclude in-home health care and personal care services. Also, these early plans always limited the amount and/or length of coverage. Many of the more recent private long term care policies provide coverage of custodial and personal care services, home care benefits, case management services, and consumer protection features such as guaranteed renewability and inflation protection. In spite of these advances, less than 2 percent of all elderly have any private long term care insurance protection and the industry is still considered in its infancy.

Medicare Catastrophic Coverage Act

In June 1988, the Medicare Catastrophic Coverage Act of 1988 was enacted. This legislation extended Medicare coverage for beneficiaries who are in a hospital or skilled nursing facility. Provision of the Act also increased home health services provided by a skilled nurse, physical therapist or speech pathologist, and the Act contained a respite care benefit whereby up to 80 hours per year of in-home care can be provided to chronically dependent Medicare beneficiaries. These and other provisions of the Act would have extended coverage for Medicare beneficiaries with AD. However, these provisions in the Act were repealed in December 1989, thus restoring Medicare benefits to those available prior to January 1, 1989 (i.e., the scheduled beginning of the Medicare Catastrophic Coverage Act).

The Medicare Catastrophic Coverage Act of 1988 also requires State Medicaid programs, on a phased-in basis, to pay Medicare premiums, deductibles and coinsurance for elderly and disabled individuals who are poor. This "buy-in" provision increases the number of people with AD who are eligible for both Medicaid and Medicare coverage (dual eligible individuals). Another important provision of the Act allows the spouse of an individual who is Medicaid eligible and institutionalized to retain some income and resources rather than becoming impoverished in paying for institutional care. This provision will provide financial relief to the spouses of many individuals with AD. Neither of these provisions was repealed by the December 1989 Repeal Act.

The most significant problems with current Medicare, Medicaid, and private health coverage are summarized below:

- While about 90 percent of all patients with AD or a related dementia are eligible for Medicare, most of the services actually required for management of the disease (i.e., long term care and personal care services) are not covered in Medicare's benefit package.

- While many, if not most, of the services required by patients with dementia and their families are covered as a benefit under the Medicaid program, most individuals with AD or a related dementia and their families must "spend down" their assets in order to become eligible for Medicaid coverage.

- While strides have recently been made in private long term care insurance, there is still limited coverage of long term care services by private insurers for persons with AD or a related dementia.

- While we are able to get estimates of the costs to the Medicare program for providing various services specifically to patients with AD and related dementias, it is much more difficult to obtain cost estimates from other third party payers (Medicaid and private health insurers) and from individulas and families affected by these illnesses.

Progress to Date

Medicaid Home and Community-Based Waivers (2176 Waiver)

Since 1982, HCFA has been granting specific waivers to States permitting Medicaid coverage and reimbursement for home and community-based services provided to individuals who would otherwise need care in a nursing home or other institutional setting. As of June 1989, 251 home and community-based waivers

have been approved in 47 States. Of these 251 approvals, 125 waivers from 47 States are currently active. Total expenditures for the program were $748 million in FY'88. Patient with AD or related dementias and their families who are eligible for Medicaid, and who are in localities and States covered under the waivers, are provided special services such as adult day care, respite care, and homemaker care management services to delay or prevent institutionalization.

Medicare AD Demonstration Projects

Section 9342 of the Omnibus Budget Reconciliation Act of 1986 requires the Secretary of DHHS to conduct at least 5 (and not more than 10) demonstration projects to determine the effectiveness, cost, and impact on health status and functioning of providing comprehensive services for individuals entitled under Medicare who are victims of AD or related disorders. The demonstration projects are mandated to be conducted over a 3-year period, to include services designed to meet the specific needs of AD patients, to be conducted by organizations that either directly or by contract are able to provide comprehensive client evaluations and additional services, and to be conducted in sites that are geographically diverse and readily accessible to Medicare beneficiaries. Services provided under the demonstration projects will include case management services, home and community-based services, mental health services, respite care and other supportive services, and counseling for the family. Consistent with HCFA's mandate under P.L. 99-660, this project will determine more accurately the costs of AD and related dementias, and the impact that persons with these disorders and their families experience when they are provided with needed services.

To finance this effort, the legislation authorizes expenditures from the Medicare trust funds of not more than $40 million for the demonstration projects and $2 million the evaluation of the projects. The legislation also requires that two reports be prepared. The first is a preliminary report to be made to Congress during the third year of the projects. This report would include a description of the services offered and the sites at which the demonstration projects are being conducted. The second is a final report which would be submitted at the completion of the demonstration and include recommendations for appropriate legislation.

In June 1988, 51 organizations and agencies from across the country, representing a wide range of public programs and health care providers, submitted applications to serve as sites in the demonstration. These applications were reviewed by HCFA's ORD to evaluate their organizational experience, familiarity with the service needs of Alzheimer's disease patients, staff

qualifications, and thoroughness and sophistication of their proposed implementation strategy.

Eight applicants were selected as demonstration sites: Monroe County Long Term Care Program, Inc., Rochester, New York; Carle Clinic, Urbana, Ilinois; Northeast Community Mental Health Center, Memphis, Tennessee; Good Samaritan Hospital and Medical Center, Portland, Oregon; Cincinnati Area Senior Services, Inc., Cincinnati, Ohio; Wood County Senior Citizens Association, Parkersburg, West Virginia; the Wilder Foundation, Minneapolis, Minnesota; and Miami Jewish Home and Hospital, Miami, Florida. These awards were made based on the results of the technical evaluation of the applications and in consideration of the need for geographic dispersion, a mix of urban and rural environments, and sites with a diversity of organizational characteristics.

The demonstation sites began their 6-month planning phase on May 15, 1989. During this phase, the sites hired and trained staff. An orientation conference with representatives from the demonstration sites, ORD, and Mathematica Policy Research, Inc., the contractor working with ORD to design and implement the demonstration projects, was held on June 28-30 in Baltimore, Maryland, to discuss demonstration goals and expectations, site reporting procedures, payment/billing for services, and case management approaches. The provision of services to clients began in December 1989.

Subsequent to receiving responses to a Request for Proposals (RFP), a contract for evaluating the demonstration project was awarded to the University of California, San Francisco, in October 1989. The evaluation will compare the relative impacts of alternative service packages on clients and families and their costs to Medicare.

New Jersey Respite Care Pilot Project

In the Omnibus Budget Reconciliation Act of 1986, Congress included a provision to establish a program to assist families in the care of elderly and disabled relatives. The New Jersey Respite Care Pilot Project was developed to determine the impact of providing respite care services both on elderly, functionally impaired care-recipients who are considered at risk of institutionalization, and on their caregivers. The project focuses on two key issues: whether respite services effectively reduce institutionalization, and whether they relieve caregivers' physical, emotional, and financial stress and enhance the role of the family in providing long term care services. Based on experience with other respite care projects supported by HCFA, it is estimated that 30 to 45 percent of the individuals enrolled in this project will have AD or a related dementia.

In compliance with the legislation, the respite care services provided under this project include: short-term and intermittent companion services; homemaker, home health aide and personal care services; adult day care, both social and medical; and inpatient respite care in a hospital or nursing home. Services are available on a planned or emergency basis. Inpatient respite is limited to a total of 14 days a year for each client. In addition to these services, peer support, training, and counseling are provided to family caregivers.

All of New Jersey's 21 counties are participating in the project. The State administers and operates the program in each county by contracting with a local provider or government agency. These designated sponsoring agencies receive a yearly budget based on that county's proportion of the target population. Expenditures for each client were limited to a maximum of $2,400 during the first year; this amount will be adjusted annually. Clients are charged a co-payment that is calculated on a sliding scale based on their income. Federal payments under this demonstration cannot exceed $2 million per fiscal year. Federal funding for this project began on July 1, 1988 and is expected to end on September 30, 1990.

S/HMO Demonstrations

S/HMO is a novel concept for financing and expanding long term care coverage benefits for Medicare patients. Through the S/HMO, Medicare pays a fixed monthly capitation amount (as in a health maintenance organization), so that beneficiaries are eligible to receive a range of home, community, and institutional long term care services, as well as medical and acute care. Approximately 5 percent of enrollees are severely impaired persons who are certified for nursing home placement based on Medicaid criteria. Four S/HMO demonstration projects were initiated in January 1985 and will operate through 1992. A contract for an evaluation is being performed by the University of California at San Francisco. Though not dealing exclusively with persons with AD per se, some findings relevant to patients and families with AD should emerge. Data on those enrollees with AD will be available for analysis in the future.

Community Care for AD and Related Disorders

HCFA approved funds for the Urban Institute in Washington, D.C. to analyze and compare data for persons cognitively impaired versus those cognitively intact who were involved in the National Long Term Care Channeling Demonstration project, conducted between 1980 and 1985. It is estimated that of the 6,000 functionally impaired patients involved in the demonstration project, 2,000 were cognitively impaired with the majority of these having AD. The two specific objectives of the

current project are (1) to determine the range of services, sources and costs of care used by community residents with cognitive impairment due to AD or related disorders and (2) to determine the risks of these residents entering nursing homes as a function of their physical and mental health status.

HCFA Plan

New Initiatives

Study of Alternative Out-of-Home Services for Respite Care

This study by Brandeis University will assess the advisability of Medicare coverage to out-of-home respite services such as those provided in a nursing home or adult day health center as an alternative to in-home respite care. The study will assess this question on the basis of cost, access, quality, and feasibility of implementation, using information available from existing data sets and ongoing respite programs and demonstrations.

National Adult Day Care Center Survey (1989)

This project will fulfill the requirements of section 208 of the Medicare Catastrophic Coverage Act to survey adult day care centers (ADCs). Specifically, this project will (1) survey ADCs across the United States, (2) develop a national listing of ADCs and a data base containing information on each of the centers, and (3) prepare a report to Congress describing the distribution of centers, their sources and funding, the services they provide, and the people they serve. The American Association of Retired Persons sponsored the data collection process and HCFA is sponsoring the data analysis and report writing. The data collection process commenced April 1989 with a survey mailing to more than 2,000 ADCs. The data analysis commenced during the summer of 1989, with a first draft of the report to be completed by late 1989. The contractor for this project is the University of California at San Francisco, with a subcontract to the National Institute of Adult Day Care (part of the National Council on the Aging).

OFFICE OF HUMAN DEVELOPMENT
Administration on Aging

Alzheimer's Disease

In FY 1989, the Administration on Aging (AoA) maintained a number of activities designed to develop and strengthen community based care for the victims of Alzheimer's Disease (AD) and their families. These activities included: AoA/NIA co-sponsored state-of-the-art conferences that focused on current practices in caregiving support for families of AD patients; collaborative efforts involving AoA, the Robert Wood Johnson Foundation (RWJF) and the Alzheimer's Association that supported a number of demonstrations in the RWJF Dementia Care and Respite Services Program; and projects designed to demonstrate better ways to provide community care for people with AD as well as their family caregivers.

AoA also continued its support of a National Long Term Care Resource Center with a focus on Alzheimer's Disease and other dementias. The Center is specifically devoted to providing training, technical assistance, short-term research, and dissemination activities for State Agencies on Aging, and others, in AD and other dementias. The Center continues to focus its assistance efforts on developing effective service programs to deal with the problems of short-term treatment and long-term management of AD patients and with the needs of family caregivers. AoA plans to continue its support of this Center in FY 1990.

AoA is also planning on including a priority area that addresses AD in its FY 1990 Discretionary Funds Program. Grant applications will be solicited to develop projects that demonstrate ways to improve access to services by minority persons with AD and their family caregivers.

Funding for Alzheimer's Disease is as follows (in thousands):

FY 1987	1,240.4
FY 1988	1,899.8
FY 1989	470.0
FY 1990	900.0*
FY 1991	$ 500.0*

* Estimated

Arthritis and Related Musculoskeletal Disorders

Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
National Institutes of Health:					
National Institute of Arthritis and Musculoskeletal and Skin Diseases	$70,634,000	$67,849,000	$71,218,000	$74,047,000	$76,420,000
National Cancer Institute	846,000	1,290,000	1,377,000	1,420,000	1,460,000
National Heart, Lung, and Blood Institute	1,203,000	953,000	636,000	650,000	675,000
National Institute of Dental Research	6,697,000	6,791,000	9,099,000	9,426,000	9,775,000
National Institute of Diabetes and Digestive and Kidney Diseases	7,450,000	7,750,000	6,140,000	6,360,000	5,750,000
National Institute of Neurological and Disorders and Stroke	2,519,000	2,637,000	2,605,000	2,691,000	2,815,000
National Institute of Allergy and Infectious Diseases	16,043,000	20,105,000	24,503,000	25,302,000	26,613,000
National Institute of General Medical Sciences	404,000	456,000	247,000	250,000	250,000
National Institute of Child Health and Human Development	1,711,000	1,397,000	1,813,000	1,900,000	2,000,000
National Eye Institute	---	---	695,000	712,000	759,000

National Institute on Aging	1,838,000	2,965,000	3,492,000	3,614,000	3,758,000
Division of Research Resources	6,924,000	5,164,000	5,070,000 1/	4,800,000 1/	4,514,000 1/
National Center for Nursing Research	---	141,000	227,000	250,000	250,000
Office of the Director 2/	144,000	167,000	205,000	---	---
TOTAL, NIH	118,415,000	119,870,000	129,330,000	133,422,000	136,059,000

1/ This includes RCMI awards. Prior to FY 1989, RCMI's were shown in OD.

2/ This includes AREA awards for FY 1987 - 1991, and RCMI awards for FY 1987 and FY 1988.
1987 AREA - NIAID $52,000; 1988 AREA - NIAMS $71,000; 1989 AREA - NIAMS $205,000.
1987 RCMI - DRR $92,000; 1988 RCMI - DRR $96,000.

NATIONAL INSTITUTES OF HEALTH

National Institute of Arthritis and
Musculoskeletal and Skin Diseases

ARTHRITIS, RHEUMATIC DISEASES, AND RELATED DISORDERS

Arthritis is a group of disorders that can strike individuals of every age and race, male or female. Although the word "arthritis" literally means joint inflammation, it is often used more broadly to indicate any of the more than 100 so-called rheumatic diseases. These diseases affect not only the joints but also other connective tissues of the body, including important supporting structures such as muscles, tendons and ligaments, as well as the protective coverings of internal organs.

Approximately 1 in 7, or more than 37 million Americans are affected by some form of rheumatic disorder. In addition, at least 24 million more have the bone-thinning disease osteoporosis, and untold millions have other musculoskeletal disorders. "Arthritis and related disorders of the musculoskeletal system including osteoporosis are the most frequently-reported cause of impairment affecting the adult population of the United States," according to the National Arthritis Workgroup convened by the National Institutes of Health and the Arthritis Foundation. The workgroup found that 32 percent of the adults in the United States are currently affected by musculoskeletal problems, with more than 50 percent of the population 65 and older affected by some form of arthritis.

The impact on individuals and society in terms of physical, emotional and financial suffering is enormous. According to the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), an estimated $35 billion annually in medical costs, lost wages, and associated economic losses may be attributable to musculoskeletal diseases. This figure is expected to rise appreciably since the largest segment of Americans at risk--the elderly--will double over the next 50 years.

NIAMS leads and coordinates the Federal biomedical research effort against the many forms of arthritis and related disorders. Other NIH components that support research in this area include the National Cancer Institute, the National Institute of Dental Research, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Neurological Disorders and Stroke, the National Institute of Allergy and Infectious Diseases, the National Institute of Child Health and Human Development (NICHD), the National Institute on Aging, the Division of Research Resources, and the National Institute of General Medical Sciences.

NIAMS Research Highlights

Although medical science has yet to find a cure for many forms of arthritis and related disorders, significant progress has been made through basic and clinical research conducted both in NIAMS intramural laboratories and, through NIAMS support, in research settings throughout the country.

Osteoarthritis

Degenerative joint disease or osteoarthritis is the most common form of arthritis, afflicting more than 16 million Americans. This disease primarily affects cartilage--the protective material that covers and cushions the ends of the bones--causing it to fray, wear, ulcerate, and, in extreme cases, to disappear entirely, leaving a bone-on-bone joint. At the edges of the joint, bony spurs may form. Disability results most often from disease in the knees, hips, and spine.

One factor often cited as a possible cause of osteoarthritis in general, and particularly of osteoarthritis in the knee, is obesity. To assess this association, researchers led by Dr. David T. Felson, Multipurpose Arthritis and Musculoskeletal Diseases Center at Boston University School of Medicine, analyzed data from the Framingham Study, which observed the population of a small Massachusetts city for more than 35 years. They found a strong association between being overweight or obese and having osteoarthritis of the knee 35 years later. The association was stronger for women than for men.

Because so many postmenopausal women are using estrogen replacements and because osteoarthritis is so common in older persons, researchers are evaluating whether this therapy predisposes women to develop the disease. Marian T. Hannan and associates at Boston University evaluated knee x-rays of 600 women, 200 of whom had used estrogen. The researchers found that estrogen use among postmenopausal women is not associated with an increased risk of osteoarthritis of the knee. In fact, estrogen use may have a modest protective effect.

Rheumatoid Arthritis

A chronic inflammatory disease of unknown cause, rheumatoid arthritis (RA) afflicts more than two million Americans, with twice as many women as men affected. The primary target of this major crippling disorder initially is the synovium (joint lining). This tissue, which normally is smooth and shiny, becomes inflamed, painful, and swollen. Rheumatoid arthritis can also produce such general symptoms as weakness, fatigue, and loss of appetite, and it can affect other parts of the body such as blood vessels. The disease tends to be both chronic and irregular, and is frequently disabling.

Studies in the laboratories of NIAMS, National Institute of Mental Health and NICHD may provide a new approach to understanding rheumatoid arthritis. According to recent studies by NIAMS intramural scientists, Dr. Ronald L. Wilder and Dr. Esther M. Sternberg and colleagues,

susceptibility to arthritis may be linked to the brain's response to and regulation of inflammation. The researchers studied two strains of rats: one that is susceptible to the induction of arthritis by injection of cells walls of bacteria and one that is not. They found that a critical defect in the susceptible rats impairs the ability of the brain's hypothalamus to produce and release a hormone critical in regulating the body's response to inflammation. Arthritis research has generally focussed on local factors at the site of joint inflammation. This study suggests a new mechanism for the disease. The researchers caution, however, that a similar defect in humans with arthritis has yet to be proven.

Low doses of methotrexate, an anticancer drug, have been found to be an effective treatment for RA patients who have not responded to conventional forms of therapy. However, long-term effectiveness and toxicity of methotrexate remain unclear. Researchers led by Dr. David E. Trentham at Beth Israel Hospital, Boston, evaluated patients with severe RA who had received methotrexate. During a trial period of 36 months, patients on methotrexate experienced a significant improvement in the number of painful and swollen joints, sedimentation rate (a measure of inflammation), and in both the physician's and patient's assessment of disease activity. Results of this trial indicate that low-dose methotrexate provides an effective treatment for RA.

Over the years, assessment of disease progression in RA has depended on repeated x-ray examination of the affected joints; this is expensive and involves exposure to radiation. Dr. Graciela S. Alarcon and her associates at the University of Alabama Multipurpose Arthritis and Musculoskeletal Diseases Center in Birmingham evaluated an alternative to x-rays, the Joint Alignment and Motion (JAM) scale. The JAM scale is a 5-point scale that assesses the percentage of motion lost and the amount of joint instability or malalignment present in patients with RA. They found that the JAM scale is a quick, inexpensive and reliable method of estimating joint motion and joint alignment, and that it correlates well with functional impairment and disease severity. This scale thus may be a good alternative to x-rays for following the long-term course of this disease.

Lyme Disease

A complex disorder, Lyme disease was first identified in 1975 by NIAMS grantee Dr. Allen C. Steere, now at Tufts-New England Medical Center in Boston. The disease is caused by a tick-borne spirochete (a form of bacteria), Borrelia burgdorferi, which was isolated in 1982 by a scientist at the National Institute of Allergy and Infectious Diseases (NIAID). Lyme disease can involve many tissues of the body, including the skin, joints, heart, and nervous system.

Lyme disease appears to have a widespread distribution in the United States and is found in many other parts of the world, including the Soviet Union. As part of the U.S.-U.S.S.R. Cooperative Program in Arthritis and Musculoskeletal Diseases, American researchers led by Dr. Steere, in collaboration with Soviet scientists, were able to identify 90 patients in

the Soviet Union with tick-borne erythema migrans (spreading, often circular skin lesions), abnormalities of the nervous system, and arthritis due to Lyme disease. Additional cooperative studies are being planned to compare clinical findings and differences between the strains of Borrelia burgdorferi in the two countries. According to Dr. Steere, "Understanding the regional variations of Lyme disease will improve diagnosis and treatment worldwide."

Early diagnosis of Lyme disease is important because treatment with antibiotics is often effective in the early stages of the disease. Unfortunately, serologic (blood) tests may be unreliable, in that antibodies (proteins that fight invading organisms) to the Lyme spirochete may not be present in the blood during the first few weeks of the disease.

Testing for the spirochete itself may prove a feasible alternative. Researchers led by Dr. Russell C. Johnson at the University of Minnesota were able to detect the Lyme spirochete in the urine of mice infected with Borrelia burgdorferi earlier and faster than they could detect antibodies in the blood. By using two different immunological techniques, ELISA and Western blot analysis, these researchers found clear differences between the urine of infected and noninfected mice. Only the urine from mice infected with Borrelia burgdorferi tested positive for the Lyme spirochete. The researchers believe that testing the urine of infected individuals may provide a rapid diagnostic method for the early and accurate detection of Lyme disease in humans.

Lupus Erythematosus

The exact cause of lupus is unknown; the evidence suggests that it may result from a disorder in the body's production of antibodies. In lupus, the body produces abnormal antibodies that react against the patient's own tissues. In its systemic form, lupus can affect many organ systems of the body.

Most victims of lupus are women of childbearing age, and there is a common belief that pregnancy causes the disease to worsen. Therefore, many physicians prescribe prophylactic prednisone therapy for lupus patients who become pregnant. Dr. Michael D. Lockshin, formerly with the Hospital for Special Surgery in New York City, and now with the NIAMS, evaluated 80 pregnant lupus patients for signs and symptoms of the disease, number of organ systems affected by the disease, and extent of organ abnormalities. During this study, patients did not receive additional therapy to prevent a flare of the disease. Dr. Lockshin found that lupus did not worsen during pregnancy; he concluded that preventive prednisone therapy is unnecessary.

Some lupus patients have a history of repeated miscarriages and, thus, are likely to have future miscarriages. Correct medical management of these patients to achieve a successful pregnancy is controversial. Dr. Leena Sharma and her colleagues at the Multipurpose Arthritis and Musculoskeletal Diseases Center at Northwestern University in Chicago developed a computerized decision model to determine the best therapy for these patients. This decision model, which utilized Dr. Lockshin's data,

incorporated various tests and treatment strategies such as prednisone, aspirin, a combination of prednisone and aspirin, and subcutaneous heparin. The researchers found that the preferred method of preventing miscarriages for these patients is either aspirin or heparin.

A reversible form of lupus also can occur in association with certain drugs, including procainamide, that are used to treat irregular heart rhythms. Most people who take procainamide for long periods of time develop antinuclear antibodies called ANA (high levels of ANA increase the chance of lupus). However, only 15 to 20 percent of these people develop lupus-like symptoms. NIAMS grantee Dr. Robert L. Rubin and associates at the Scripps Clinic and Research Foundation in La Jolla, California, measured specific antibodies to a certain histone complex known as H2A-H2B in three groups of people: patients with procainamide-induced lupus, patients with lupus induced by other drugs, and normal controls. Histone is a protein closely linked to DNA. Only the procainamide-induced lupus patients had elevated antibodies to this histone complex. Measurements of this specific antibody may prove to be a good indicator of procainamide-induced lupus.

Sjogren's Syndrome

An autoimmune disorder, Sjogren's syndrome is characterized by dryness of the eyes and mouth caused by destruction of the glands that produce tears and saliva. It may be a primary disease or it may be secondary to certain rheumatic diseases, such as rheumatoid arthritis, scleroderma, or systemic lupus erythematosus. In some cases, Sjogren's patients may develop lymphoma (cancer of lymphoid tissues).

The aims of treatment for the disorder are relief of symptoms and treatment of the underlying immune dysfunction occurring in primary Sjogren's syndrome. Drugs used for treating the associated autoimmune diseases (such as rheumatoid arthritis and lupus) are often effective for patients with Sjogren's syndrome. Dr. Robert I. Fox and coworkers at the Scripps Clinic and Research Foundation compared patients who were given hydroxychloroquine (Plaquenil) for a 12-month period to those receiving other forms of therapy. Hydroxychloroquine was found to diminish levels of circulating antibodies and to decrease inflammation and disease activity. In addition, lymphocytes (white blood cells involved in immune defenses) removed from treated patients showed a decrease in autoantibody production.

Scleroderma

Scleroderma, which literally means "hard skin," is also known as progressive systemic sclerosis (PSS). Scleroderma is a connective tissue disorder in which excessive amounts of the protein collagen accumulate in the skin. It is also a disease of the vascular (blood vessel) and immune systems and it can impair the function of internal organs such as the kidneys, lungs, heart, or gastrointestinal tract. Two clinical subsets of scleroderma are diffuse scleroderma (widespread skin thickening and internal organ involvement) and CREST syndrome. CREST is an acronym for specific features of scleroderma: calcinosis (accumulation of calcium

below the outer layer of skin), Raynaud's phenomenon (vasospasm), esophageal dysfunction (difficulty in swallowing), sclerodactyly (tight skin on the fingers), and telangiectasia (dilated, visible small blood vessels).

Patients with scleroderma may develop circulating autoantibodies that can be used as markers for the disease. Dr. Sergio A. Jimenez at the Thomas Jefferson University and Dr. Gerd Maul of The Wistar Institute in Philadelphia have developed a new sensitive test to distinguish patients with diffuse scleroderma from those with CREST syndrome. Using recombinant DNA methods, they tested blood from normal subjects and patients known to have either diffuse scleroderma, CREST syndrome, or systemic lupus erythematosus. The investigators used antibodies to two specific antigens, topoisomerase 1 and kinetochore, known to be associated with diffuse scleroderma and CREST syndrome respectively. They found that 74 percent of CREST cases reacted with the kinetochore antigen, and 48 percent of the diffuse scleroderma cases reacted with the topoisomerase 1 antigen. Using these methods, they were able to identify 50 percent more positive cases of diffuse scleroderma than with previous tests. Both normal subjects and lupus patients did not react with the antigens.

Ankylosing Spondylitis

A type of arthritis that primarily affects the spine, ankylosing spondylitis (AS) is found mainly in young Caucasian males between the ages of 16 and 35, and in some women. Researchers have known for several years that there is a strong association between the different forms of arthritis and the genetic marker HLA-B27 in 90 percent of white patients with the disease. The evidence suggests that the disease occurs when an individual bearing a predisposing gene, such as HLA-B27, is exposed to an environmental triggering factor, such as a bacterium or a virus.

Infection by bacteria, such as Salmonella and Klebsiella pneumoniae, has often been known to precede the onset of ankylosing spondylitis. But, exactly how HLA-B27 is involved in the development of ankylosing spondylitis is unknown. Dr. Ralph C. Williams, Jr. and colleagues at the University of Florida Medical School in Gainesville obtained inflamed synovial joint tissues from HLA-B27 positive patients with ankylosing spondylitis and synovial tissues from patients with other rheumatic diseases. The researchers then exposed these tissues to antibodies to Klebsiella pneumoniae, and found that only the HLA-B27 positive tissues exhibited a strong reaction to the antibody. These and other findings suggest that bacterial antigens such as those found in Klebsiella or [illegible]er similar organisms may be very similar to those found in the HLA-B27 molecule. This is termed "molecular mimicry", and it means that a bacterial infection may initiate an immune reaction that would be perpetuated as an autoimmune reaction directed towards a molecularly similar substance (HLA-B27) that was present in the body. Research on genetic markers may eventually lead to a better understanding and improved treatment for ankylosing spondylitis and other forms of HLA-B27 positive disease.

Orthopedic Research

The adult skeleton is in a dynamic state of bone turnover that is normally in balance. Bone, like any other tissue of the body, is constantly being rebuilt, or "remodeled". Old bone is torn down--resorbed--and then replaced with new bone.

Because there is an increased awareness that even moderate exercise such as walking can help maintain bone mass as we age, information on how bone responds to mechanical loads incurred through exercise is an important step in understanding bone remodeling. NIAMS grantee Dr. Albert J. Banes and associates at the University of North Carolina, Chapel Hill, have developed an innovative method to "exercise" cells in culture. The researchers subjected chick osteoblast-like (bone forming) cells to a cyclic strain (intermittent strain and rest) at the rate of three cycles per minute for 8 hours. They found that cells altered their position perpendicular to the direction of the load. After 3 days of cyclic strain, the osteoblast cells responded to their environment by dividing and mineralizing. Researchers said that these new findings may provide the tools to explore how exercise has a positive impact on building bone.

Osteoporosis

In osteoporosis ("porous bone"), bone mass decreases, making bones more susceptible to fracture. Osteoporosis is the leading cause of bone fractures in postmenopausal women and in elderly persons in general. It is estimated that osteoporosis and osteoporotic fractures cost the Nation more than $7 to $10 billion annually, with at least two-thirds of this cost incurred because of hip fractures.

Bone mass at any age is dependent upon a complex interaction of genetics, physical activity, nutrition and hormones. Studies have shown that estrogen replacement therapy may retard bone loss in postmenopausal women. The effect of calcium intake on bone loss is also of interest. Researchers led by Dr. Rivka B. Sandler at the University of Pittsburgh in Pennsylvania studied 174 postmenopausal women in order to assess the effect of estrogen and calcium on the radius (wrist bone). Examination of women who reported a high life-time intake of calcium revealed that it had a protective effect on bone. Women with a combination of high estrone (a type of estrogen) levels and high calcium levels had significantly greater bone density than with those with less calcium and/or estrone. Researchers suggest that a lifetime of adequate calcium intake coupled with adequate levels of estrogens could maximize bone density after menopause.

Black men and women have a lower incidence of osteoporosis and hip fractures than do white men and women. Research has shown that the mineral content of bone in blacks is 5 to 10 percent higher than in whites. The reason for this difference has not been determined.

Dr. Norman H. Bell and associates at the Medical University of South Carolina in Charleston studied a group of 25 normal subjects, composed of

12 blacks and 13 whites, with a nearly equal balance between men and women in both groups. The researchers found that the rate of bone turnover or remodeling is lower in blacks than in whites. According to the researchers, a diminished rate of skeletal remodeling or slow bone turnover in black adults may protect the skeleton from the more rapid bone loss that characterizes the early stages of osteoporosis in whites.

Tendons and Ligaments

Tendons are fibrous cords that connect muscles to bone. Tendinitis, or inflammation of tendons, may occur with overuse. Professional musicians, especially pianists, frequently develop tendinitis and pain in their fingers and hands that may impair their performance or even terminate a career.

A research team led by Dr. Kenneth D. Brandt at the Indiana University Multipurpose Arthritis and Musculoskeletal Diseases Center in Indianapolis utilized a computerized electronic piano to study various finger techniques used by healthy musicians; it enabled the researchers to compute the amount of force applied to the fingertips during playing. Applying this information, they developed a mathematical model of optimal finger positions that would minimize the tensions in tendons and stresses on joints during piano playing. According to the researchers, information gained from this type of analysis may be applied to prevention and treatment of a variety of performance-related hand problems in musicians, as well as assembly line workers, and others in jobs requiring intensive hand motion.

The injury to and the healing of tendons and ligaments are also important in sports-related activities and trauma. Ligaments, which are bands of tissue that connect bone to bone across the joint, have long been considered to be dense fibrous tissue with very few distinctive characteristics. However, when injuries occur, there is a difference among ligaments in the healing process. For example, the medial collateral ligament (MCL), found in the inner side of the knee, heals rapidly even without surgery. The anterior cruciate ligament (ACL), found within the joint itself, heals very slowly, even when repaired surgically.

Dr. Wayne H. Akeson and his associates at the University of California in San Diego found that, architecturally, MCL and ACL ligaments are very different, thereby accounting for the differences in healing. The MCL ligament has a good blood supply with a cell type similar to that seen in healing skin, whereas the ACL ligament has a cartilage-like cell that cannot regenerate itself. This finding is highly important, because we now know that treatments must be individualized for a specific ligament to heal properly.

Exercise

Most experts believe that peak bone mass, usually attained by the age of 35, is the key to determining how susceptible a person will be to fractures later in life. The roles of physical activity and nutrition, such as calcium intake, in determining adult peak bone mass have not been

fully elaborated. Dr. Robert Lindsay and his associates at the Specialized Center for Research in Osteoporosis at the Helen Hayes Hospital in West Haverstraw, New York, examined bone mineral density in both the forearm and the spine of 60 healthy Caucasian women (ages 25 to 34), whose nutrition and life-style varied considerably. They found that physical activity, such as running and walking, increased bone mineral density in the spine. On the other hand, forearm bone mass was not related to physical activity; however, it was significantly improved by a daily calcium intake of 800 to 1000 mg/day.

Increased participation in physical fitness and exercise by an older population has led researchers to investigate weight bearing exercise, such as running, and its effect on bone mass. Dr. Beat A. Michel and associates at Stanford University Medical Center, Palo Alto, California, studied 78 male and female runners over age 50 to determine the impact of weight-bearing exercise on bone mineral content of the lumbar (lower) spine. They found a strong correlation overall between exercise--up to five hours a week--and an increase in bone density in the lumbar spine. However, unexpectedly, runners over age 65 who exercised above these levels had a surprisingly low bone density. The researchers conclude, therefore, that moderate weight-bearing exercise may increase bone density in the lumbar spine, but overexercise actually may be harmful in the elderly.

National Cancer Institute

This year, the National Cancer Institute contributed to advances in arthritis research through studies of growth of new capillary blood vessels, which is a characteristic of rheumatoid arthritis, and of immune system interactions that may contribute to development of the disease.

Rheumatoid arthritis, diabetes retinopathy, tumor growth and spread, and certain other conditions are often associated with persistent growth of new capillary blood vessels, or angiogenesis. Researchers are interested in finding ways to safely inhibit angiogenesis and see if this has a beneficial therapeutic effect. (In healthy adults, angiogenesis does not usually occur except during wound repair, menstruation, and formation of the placenta.)

This year, NCI grantee Dr. Judah Folkman at the Harvard Medical School and Children's Hospital in Boston, Massachusetts, and colleagues discovered a new synthetic compound that, when combined with cortisone, inhibited the growth of new capillary blood vessels. The compound itself does not inhibit blood vessel growth but acts as a carrier, transporting cortisone (or potentially other steroids or agents with antiangiogenic properties) to the cells that line blood vessels, where the antiangiogenic action is most effective.

The synthetic compound, B-cyclodextrin tetradecasulfate, when given with cortisone, inhibited angiogenesis 100 to 1,000 times better than heparin in a chick embryo bioassay. This finding suggests that the synthetic compound is an effective substitute for heparin which, when administered with steroids with antiangiogenic properties, can inhibit angiogenesis. Not all investigators have found that heparin augments the effects of antiangiogenic steroids, however, perhaps because heparin preparations have not been uniform. The compound has a comparatively simpler chemical structure than heparin.

Studies have suggested that interactions between T cells, a type of immune system cell, and cells of the synovium, the protective lining of joints that becomes inflamed in rheumatoid arthritis, may be important in the development of the disease. Researchers have found cell adhesion molecules that mediate interactions between T cells and cells of the synovium.

Grantees Dr. Laura Hale and Dr. Barton Haynes at Duke University School of Medicine in Durham, North Carolina, and Dr. Timothy Springer at Harvard Medical School and Dana-Farber Cancer Center in Boston, and colleagues investigated the types of synovial cells that use the cell adhesion molecules ICAM-1 and LFA-3 to bind to T cells. They found adhesion molecules on several types of synovial cells suggesting that T-cell interactions with numerous types of cells in the synovium could occur and participate in chronic synovial inflammation.

National Institute of Dental Research

The National Institute of Dental Research (NIDR) supports a wide range of projects related to arthritis, including laboratory and clinical studies on modulating pain and reducing inflammation and basic research on understanding the factors involved in the development of rheumatoid arthritis and osteoarthritis.

Inflammatory Pain Is Reduced by Local Injection of Pain Killers

Dr. Ronald Dubner and other investigators in the NIDR intramural laboratories have demonstrated that injection of opioid drugs directly into the site of inflammation can relieve pain and bypass the need for high systemic doses of these drugs, which can cause undesirable side effects. This finding, based on studies using a rat model, paves the way for developing and testing opiate drugs that can be injected into inflamed human joints to ease the pain of rheumatoid arthritis. In related research, these investigators have discovered that opiates such as morphine decrease the amount of heat and swelling at the inflammation site, suggesting that opiate drugs not only relieve pain but also can help reduce inflammation.

Interferon and Tetracycline Reduce Inflammation

NIDR intramural scientist Dr. Sharon Wahl and colleagues have discovered that the protein gamma-interferon, which is generated by the immune system, reduces inflammation in rats having a condition similar to rheumatoid arthritis. Additional studies by intramural investigator Dr. Larry Wahl indicate that this protein also blocks monocytes, or white blood cells, from generating the enzyme collagenase, which plays a key role in the destruction of joint tissue.

In related work, Dr. Lorne Golub, an NIDR grantee at the State University of New York at Stony Brook, has found that the antibiotic tetracycline also can inhibit collagenase production. He followed up on this finding by altering tetracycline to remove its antibiotic properties while retaining its ability to hinder production of the enzyme. Preliminary clinical studies with RA patients show that the chemically modified tetracycline substantially limits harmful collagenase activity in the fluid of their joints.

Researchers Discover Autoantibody-Secreting Cells

Intramural researcher Dr. Paolo Casali and colleagues, including NIAMS scientist Dr. Ronald L. Wilder, have discovered a subgroup of white blood cells in normal, healthy individuals that can be stimulated to generate rheumatoid factor, an antibody that can destroy the body's own tissue. Activation of these B cells by such factors as viruses, oncogenes, or growth factors may play a critical role in the development of rheumatoid arthritis.

Transforming Growth Factor-Beta Plays a Role in Arthritis

Dr. Sharon Wahl and other NIDR intramural investigators are moving closer to an understanding of the pathogenesis of arthritis. They have recently shown that transforming growth factor beta (TGF-beta), when injected into the joints of experimental animals, leads to the accumulation of large numbers of mononuclear cells in the synovium, or joint lining. These cells release other inflammatory cell products (cytokines) that stimulate the division of synovial cells, causing the joints to swell and fill with inflammatory cells and fluid. When administration of TGF-beta is stopped, the inflammatory response gradually declines. TGF-beta thus appears to be a key cytokine in the recruitment and activation of inflammatory cells, and regulation of TGF-beta may offer a means for effectively treating RA.

TGF-beta is released by platelets after injury, attracting white blood cells, in particular monocytes, into the site of inflammation. TGF-beta then stimulates monocytes to express other cytokines and growth factors. Dr. Wahl and her colleagues have shown that, in response to transforming growth factor beta human peripheral blood monocytes express increased levels of messenger RNAs encoding for interleukin-1, platelet-derived growth factor, fibroblast growth factor, and tumor necrosis factor. Each of these molecules plays an important part in regulating the inflammatory response. Excessive production of these products may contribute to chronic inflammatory lesions and connective tissue destruction. Continued production of TGF-beta, which appears to be a central component in this network, may contribute to the overproduction of other growth factors. Intramural studies will continue to elucidate these mechanisms in order to better understand the disease process and to provide a basis for immunotherapy.

National Institute of Diabetes and Digestive and Kidney Diseases

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducts and supports research in a variety of disease areas related to arthritis and related rheumatic disorders. These areas include endocrinology and nutrition related to osteoporosis; kidney and blood-cell abnormalities in rheumatic diseases such as systemic lupus erythematosus; disturbances of immune function; and studies on collagen and calcium metabolism, transport, absorption, and resorption.

Dietary Calcium Increase May Prevent Bone Loss

Recent studies by NIDDK grantee Dr. Daniel T. Baran and colleagues at the University of Massachusetts Medical School in Worcester have shown that an increased intake of dairy products prevented bone loss in a group of healthy premenopausal women followed at 6-month intervals over a 3-year period.

The investigators studied the effect of dairy product consumption on vertebral bone mass in 37 premenopausal women between the ages of 30 and 42. The women were similar in weight, baseline bone density, and calcium and caloric intake. Twenty women altered their diet by increasing calcium intake an average of 610 mg daily, while 17 served as controls. In the 20 women who increased their intake of dairy foods, the scientists found that vertebral bone density remained stable over the study period. In contrast, the 17 women who served as controls experienced significant bone loss: just under 3 percent, or about 1 percent each year of the study. Although the women in the experimental group ate more dairy products and thus more fat, they had no significant changes in total cholesterol, low-density lipoprotein, or high-density lipoprotein levels.

These studies suggest that increased calcium intake in premenopausal women with ample estrogen levels may prevent age-related bone loss and decrease the incidence of osteoporosis.

Defect in Parathyroid Hormone Secretion May Cause Bone Thinning

Osteoporosis, a weakening of the bones due to decreased bone mass, has been called a "silent" disease because it often progresses without any symptoms. Several hormones, including estrogen and parathyroid hormone, are involved in bone metabolism. The parathyroid gland secretes parathyroid hormone, which contributes to bone strength by regulating calcium. Parathyroid hormone not only acts directly on bone but also stimulates the conversion of vitamin D from an inactive to an active form. Vitamin D stimulates increased intestinal absorption of calcium and phosphorus and may also have a direct effect on bone.

NIDDK grantees Dr. John P. Bilezikian and Dr. Shonni J. Silverberg at the College of Physicians and Surgeons, Columbia University in New York City, and their colleagues have shown that a defect in the parathyroid gland may cause bone thinning in postmenopausal women. The researchers based their findings on evaluations of the parathyroid gland in 18

postmenopausal women. Because phosphate stimulates the parathyroid to secrete parathyroid hormone by reducing the blood calcium, the investigators administered phosphate to eight postmenopausal women with osteoporosis (mean age of 63) and to ten age-matched healthy postmenopausal women (mean age of 61). Parathyroid hormone levels rose 2.5-fold in the control group but rose by only 43 percent in the women with osteoporosis. The osteoporotic women experienced a marked reduction in vitamin D due, in part, to the abnormal parathyroid gland responsiveness. The researchers conclude that some patients with osteoporosis may have a distinct abnormality in parathyroid hormone secretion. These findings may lead to new methods for treating osteoporosis, which could be aimed at improving the ability of the parathyroid to compensate for calcium loss.

National Institute of Neurological Disorders and Stroke

The National Institute of Neurological Disorders and Stroke (NINDS) supports research to advance understanding of the role of the nervous system in arthritis. Although arthritis is generally held to be a disease of the immune system, substantial evidence implicates the nervous system as an important contributor to arthritis damage.

Dr. Allan I. Basbaum and Dr. Jon D. Levine, NINDS grantees at the University of California at San Francisco, have recently shown that peripheral nerves that carry messages back and forth between the spinal cord and the extremities are involved in the characteristic feature of arthritis: inflammation of joints. Stimulation of these peripheral nerves may cause blood vessels to dilate and leak inflammatory substances into the tissue around the joint, causing swelling. This process is called neurogenic inflammation.

Both the sensory nerves of the peripheral nervous system (which send messages about pain to the brain) and the sympathetic nerves (which carry messages from the brain to glands and other parts of the body that are not under voluntary control) appear to contribute to neurogenic inflammation. By exciting sensory and sympathetic nerve cells and the histamine-containing mast cells of the body's connective tissue, Dr. Basbaum and Dr. Levine were able to establish the sequential order of interaction among these various contributors to the inflammatory process. When the investigators excluded the sensory nerves from stimulation, the only inflammatory effects lost were those seen when sensory cells are stimulated. By eliminating mast cells, the scientists prevented the effects usually seen by exciting either sensory nerve or mast cells. Finally, eliminating only the sympathetic nerves prevented the effects of stimulating any of these cell systems. This suggests that the effects mediated by sensory nerves and mast cells are dependent upon the presence of sympathetic nerve fibers and clearly implicates the sympathetic system as a critical component of neurogenic inflammation.

Neuroimmunological Mechanisms Involved in Arthritis

For reasons not yet understood, nervous system lesions may affect the expression of arthritis. For example, osteoarthritis typically develops on both sides of the body; but in stroke survivors it develops unilaterally, sparing the paralyzed extremities. Similarly, people paralyzed by nervous system trauma who later develop rheumatoid arthritis rarely suffer the characteristic joint inflammation or erosion in the paralyzed limbs. In rats, experimentally induced arthritis is delayed in onset and diminished in severity on the side on which the sciatic nerve is cut.

Dr. Michael A. Moskowitz, a NINDS grantee at Massachusetts General Hospital in Boston, is working with Dr. Basbaum and Dr. Levine to determine the factors causing these phenomena. Building on earlier work demonstrating that substance P--a peptide believed to be involved in the transmission of pain impulses to the brain--is associated with many of the physiological changes seen in acute inflammation, the investigators

recently demonstrated that destruction of nerves containing substance P weakens the body's inflammatory response.

The research team found that substance P is more highly concentrated in the ankle, a joint considered at high risk for arthritis, than in the knee, a lower risk joint. They also discovered that nociceptive neurons--nerves that are excited only by intense, potentially harmful stimuli and that transmit pain information to the central nervous system--are more numerous, and respond at lower thresholds of stimulation, in ankles than in knees.

When the investigators used capsaicin, a drug derived from hot chili peppers, to deplete substance P in nerves of arthritic rats, they observed an increase in the threshold at which the nociceptive neurons became active. The severity of joint injury in arthritis appears to be affected by both the number of nociceptive neurons and the ongoing release of substance P into the joints. The scientists hypothesized that altering levels of substance P in the joints might modify the disease.

To gain a fuller picture of the systems at work in arthritis, this research team also studied the role that sympathetic neurons play in joint inflammation and injury. The scientists injected arthritic rats with guanethidine, a potent drug usually used to treat high blood pressure by affecting the sympathetic nervous system; in another group of rats, they injected reserpine, another antihypertensive and sedative, before inducing arthritis. In both studies, arthritic damage to the hindlimb joints--as seen by x-rays--was less than in untreated animals. The investigators attribute the reduced damage to decreased interaction between sympathetic and sensory nerves of the peripheral nervous system.

To learn whether interrupting the sympathetic nerve pathways could benefit humans, Dr. Basbaum and Dr. Levine gave arthritis patients either guanethidine or a placebo. After 14 days, the patients who had received the drug had significantly less pain and more strength than the placebo-treated group.

National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases (NIAID) supports research in arthritis because some forms of the disease, such as that resulting from Lyme disease, are triggered by infectious agents; other forms such as rheumatoid arthritis involve autoimmune processes.

In the later stages of infection with Borrelia burgdorferi (the spiral-shaped bacterium or spirochete that causes Lyme disease), chronic neurologic, cardiac, and arthritic symptoms can develop. Some people with Lyme disease who have been treated and whose symptoms seemed to have resolved can also later have unexpected flare-ups.

A clue to how the Lyme disease bacteria can persist or temporarily "go underground" to cause these problems has been found by a team of intramural investigators led by Dr. Tom G. Schwan at NIAID's Rocky Mountain Laboratories in Hamilton, Montana. They have found that the tiny spirochete gradually transforms its appearance and thus may outwit the immune system.

Like other infectious organisms, the Lyme disease spirochete has unique molecular markers, called antigens, that identify it like a fingerprint. Upon first encountering the spirochete, the immune system stimulates cells to make molecules, called antibodies, that are complementary-shaped to the Lyme disease spirochete antigens. These custom-made antibodies can lock onto the spirochetes' antigens and initiate the process that destroys the bacterium.

Working with one of the primary natural hosts of the spirochete, the white-footed mouse, Schwan and his coworkers demonstrated that the spirochete's antigenic character changes over time. As the spirochete's disguise evolves, the antibodies originally made to fight the organism no longer "fit" its antigens. By continually evolving, the spirochete can keep one step ahead of the immune system, even though in time new antibodies are made. This may explain why arthritis associated with Lyme disease appears late in the course of infection, or why it may recur even after treatment appears successful.

Interferon is Important in Rat Model of Rheumatoid Arthritis

While the cause of rheumatoid arthritis remains unknown, most scientists believe that the disease involves autoimmune processes--the immune system mistakenly attacking the body's own tissues. At Stanford University in Stanford, California NIAID grantee Dr. Hugh O. McDevitt and his coworkers are studying autoimmune arthritis in rats as a model for human rheumatoid arthritis.

To better understand how autoimmune arthritis develops in rats, the researchers conducted experiments focusing on an important chemical messenger, gamma interferon, secreted by T cells, which orchestrate the immune response. Rats with various stages of autoimmune arthritis were injected with gamma interferon, and its effects were noted. The study showed that gamma interferon caused the disease to either get worse

or get better, depending on when during the course of the disease the chemical was introduced.

The researchers concluded that clinical trials testing gamma interferon for any multistage illness like rheumatoid arthritis need to be designed and evaluated carefully to consider possible contradictory, time-dependent effects of this chemical.

National Institute of Child Health and Human Development

The National Institute of Child Health and Human Development (NICHD) supports research on the causes, early detection, treatment, and prevention of arthritis and other diseases affecting the bones, cartilage, and muscle.

Because rheumatoid arthritis is a relatively common disease in females and since many women use an oral contraceptive for birth control, the relationship between hormones and this disease is being studied by Dr. Thomas Koepsell at the University of Washington in Seattle. The study is designed to determine whether birth control pills can reduce a woman's chances for contracting rheumatoid arthritis. Preliminary analyses indicate that current pill use does protect women against the disease, but past pill use does not have any beneficial effect.

NICHD intramural scientist Dr. Alfred Yergey has invented a technique to safely measure how rapidly the body uses calcium. The new method, which differs from other tracking methods in that it requires no radioactivity, relies on a machine called a mass spectrometer. Doctors will now be able to learn more about how children grow and how aging bones become brittle. The new technology will have far-reaching effects, as information gathered by the mass spectrometer will be used to design diets for pregnant and lactating women, improve baby formulas, and help predict osteoporosis.

National Institute on Aging

The National Institute on Aging (NIA) supports biomedical, social, and behavioral research and training that relates to aging processes, specific diseases common in old age, and other special needs and problems of the older population.

New Grading Scale is Developed to Assess OA in the Hands

NIA intramural scientists Dr. Jordan D. Tobin and Dr. Douglas A. Kallman of Gerontology Research Center (GRC) in Baltimore, Maryland have developed a grading scale that is more accurate in diagnosing osteoarthritis (OA) of the hand than assessment methods previously used. This new method is especially important because the scale used before (the Killgren/Lawrence scale) was unable to assess many of the joints in the hand.

The investigators developed the new grading scale with the aid of male volunteers from the Baltimore Longitudial Study on Aging, GRC's ongoing study to assess the aging process of healthy adults. Radiographic examinations of the hand of 177 participants were made over a period of 20 years and then analyzed using the Killgren/Lawrence scale and the newer grading scale. Dr. Tobin and Dr. Kallman found the newer scale had a higher degree of accuracy in making the initial diagnosis, in determining the prevalence of specific joint abnormalities, and in characterizing the progression of the disease--all factors that will help physicians treat the growing number of older patients.

Osteoarthritis and Rheumatoid Arthritis Have an Impact on Daily Activities

The debilitating impact of arthritis on an older person's ability to function is well documented. Little is known, however, about the impact of differenct types of arthritis on an individual's ability to perform his or her daily activities. In a recent study, NIA-supported researcher Dr. Edward H. Yelin at the University of California at San Francisco has found that while OA had a negative effect on some activities evaluated, rheumatoid arthritis (RA) had a negative impact on all such activities. These included household chores, shopping and errands, social relationships, leisure pursuits, religious activities, public or volunteer work, and employment.

Dr. Yelin's 5-year longitudinal study involved 825 persons aged 50 and over who were diagnosed with OA or RA. The patients were randomly selected from the practices of Northern California reheumatologists and were compared with healthy individuals of the same age and sex who were living in the same community.

When patients were compared with people without arthritis, patients with RA experienced greater loss in all studied activities, and patients with OA experienced greater loss in only some activities (i.e., performing household chores, shopping and errands, and leisure activities). Thus, the study confirms that OA and RA can limit an individual's ability to function in later years, but that RA takes an ever greater toll than OA.

Division of Research Resources

The Division of Research Resources (DRR) supports and conducts research into arthritis at research facilities across the United States. One area of study is Lyme disease.

Although antibiotics are usually effective early in the course of the disease, longer courses of therapy are often needed later as the illness progresses. Some patients do not respond at all. The reason may be that the causitive bacteria, the spirochete Borrelia Burgdorferi, are able to evade destruction by residing inside cells. According to DRR grantee Dr. D. Denee Thomas and co-workers at the Bowman Gray School of Medicine in Winston-Salem, North Carolina, laboratory tests indicate that the organism can penetrate cells and could theoretically use the cell as a shelter from the body's immune response. Studies conducted by the researchers showed that the bacterium can penetrate the the membranes of cultured endothelial cells, pass into the cytoplasm, and then exit the cells.

Dr. Thomas believes her research into Lyme disease may have profound implications for its clinical course. The findings may explain why patients with Lyme Disease experience asymptomatic periods. Further, they suggest that a therapy capable of blocking the initial interaction of the spirochete with the host cell may prevent the disease from progressing.

Studies aimed at understanding the mechanism of disease hold the promise of leading to the development of preventive or therapeutic measures. Noting that interleukin-6 (IL-6), a protein released by cells of the immune system, may also play an important role in joint inflammation, particularly in patients with rheumatoid arthritis, DRR grantee Dr. Martin Lotz and his colleagues at the Scripps Clinic and Research Foundation in LaJolla, California, examined IL-6 production by cultured joint tissue. They also analyzed joint fluid for the presence of this protein. Using specialized laboratory services available in the Scripps General Clinical Research Center (GCRC), the grantees found that the tissue is a potent source of IL-6 and that this chemical can contribute significantly to the inflammatory response that accompanies various forms of arthritis.

Studies at the Scripps GCRC have led investigators to conclude that IL-6 can be used to monitor the development of rheumatoid arthritis and patient response to treatment. Documenting the protein's role in the onset of arthritis also explains key findings of clinical and laboratory tests on arthritic patients. Eventually, says Dr. Lotz, it may be possible to develop new therapeutic approaches to inhibit the effects of excessive IL-6 production.

Outlook

In recent years, medical science has made important advances in the field of arthritis, rheumatic diseases and related disorders. Scientists have identified the cause and developed treatments for Lyme disease, improved survival rates for systemic lupus erythematosus, and demonstrated that estrogen replacement may retard the progress of osteoporosis. Building on the knowledge that exists today, researchers are increasingly confident that they can discover the specific causes of many forms of arthritis and related musculoskeletal disorders and develop new and effective methods for preventing and treating them. The Federal government and private health organizations have developed a strong and enduring partnership committed to research and major advances on these diseases.

CENTERS FOR DISEASE CONTROL

National Center for Health Statistics

ARTHRITIS

Osteoarthritis and disc degeneration of the spine are major causes of disability in terms of limitation of activity and mobility among many people. Information on the prevalence of arthritis of the knee, hip, and sacroiliac joint has been published from the first National Health and Nutrition Examination Survey. Findings indicate that over 600,000 persons between the ages of 65 and 74 years have moderate to severe osteoarthritis of the knees. About 80 percent of those persons are women. The second National Health and Nutrition Examination Survey included x-rays of the cervical and lumbar spine for persons ages 25-74 years (women under age 50 did not have x-rays of the lumbar spine). These data are presently being analyzed to determine the prevalence of disc degeneration of the spine. In the third National Health and Nutrition Examination Survey, which began in October of 1988, information will be collected on the prevalence of osteoarthritis and rheumatoid arthritis of the hands and wrists and of the knees for persons 60 and above. This information will be used to update National prevalence estimates and to provide a baseline population for follow-up studies.

During 1980 the National Health Interview Survey collected data on musculoskeletal conditions in the civilian, noninstitutionalized population of the United States. The estimated number of conditions of known arthritis was 27,772,740 or 127.4 conditions per 1,000 persons. Of these conditions, 20.7 percent caused limitation of activity, 10.8 percent caused one or more bed days in the past year, and 62.1 percent resulted in one or more physician visits in the past year. In 1988, the estimated number of known arthritis conditions was 31,292,000 or 129.9 per 1,000 persons per year.

According to the 1987 National Hospital Discharge Survey, an estimated 430,000 patients were hospitalized in short-stay hospitals in the United States with a first-listed diagnosis of arthritis. Their average length of stay was about 8.0 days. Almost 59 percent of these patients were women and 73 percent of the patients were 45 years and older. About 53 percent of the 430,000 patients had a specific diagnosis of osteoarthritis and allied conditions. There were an additional 1.1 million diagnoses of arthritis that were not first-listed. Although some of these were additional diagnoses for the patients with first-listed arthritis diagnosis, the majority of these 1.1 million diagnosis, the majority of these 1.1 mission diagnoses were secondary to other diagnoses.

Arthritis - Con't.

In addition to the figures above, patients with a first-listed diagnosis of spinal arthritis (ankylosing spondylitis and spondylosis and allied disorders) totaled 98,000 discharges in 1987. There were an additional 199,000 secondary diagnoses of spinal arthritis in 1987.

CYSTIC FIBROSIS
Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
National Institutes of Health:					
National Institute of Diabetes and Digestive and Kidney Diseases...	$8,483,000	$9,924,000	$10,375,000	$10,650,000	$11,100,000
National Cancer Institute.....	---	11,000	---	---	---
National Heart, Lung and Blood Institute.....	3,929,000	6,933,000	6,940,000	7,100,000	7,400,000
National Institute of Dental Research.....	6,584,000	7,331,000	7,588,000	7,861,000	8,152,000
National Institute of Allergy and Infectious Diseases.....	7,782,000	7,910,000	9,804,000	10,017,000	10,572,000
National Institute of General Medical Sciences.	50,000	50,000	50,000	50,000	50,000
National Institute of Child Health and Human Development.....	---	93,000	109,000	115,000	120,000
National Institute of Environmental Health Sciences...	---	121,000	112,000	116,000	121,000
National Institute of Arthritis and Musculoskeletal and Skin Diseases.	---	162,000	162,000	168,000	177,000
Division of Research Resources.....	687,000	870,000	907,000	942,000	939,000
Office of the Director.....	70,000	---	---	---	---
Total, NIH.....	27,585,000	33,405,000	36,047,000	37,019,000	38,631,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Diabetes and
Digestive and Kidney Diseases

CYSTIC FIBROSIS

This year marks the most important discovery in cystic fibrosis (CF) research since the disease was first identified as a distinct syndrome 50 years ago. Scientists supported by the National Institute of Diabetes and Digestive and Kidney Diseases reported identifying the gene that is defective in CF, the most common lethal genetic disease in Caucasians.

The discovery of the CF gene epitomizes how basic research aimed at answering fundamental questions about the function of living organisms can provide the knowledge needed to solve long-standing medical puzzles. Scientists spent decades in a largely fruitless search for an underlying cause for CF. Then in the late 1970s, the search was energized by an explosion of knowledge in genetics, cell biology and molecular biology, which yielded powerful new ways of examining disease mechanisms. These techniques permitted scientists first to identify an abnormality in CF-affected tissues, and then to find the gene that controlled this defect.

The advance is important in two ways. First, it provides a key to fully characterizing how CF causes chronic lung and digestive disease, and to developing new, more effective treatment for this devastating disease. An estimated 1 in 20 (5 percent) Americans carry the gene for CF. Children who inherit the gene from both parents--about 1 in 2,000 newborns--face years of chronic lung disease, recurrent hospitalizations, and usually declining health. Although the advent of antibiotics greatly increased the average life expectancy of CF patients, about half of these children still die by their mid-twenties.

Second, this discovery is a milestone in genetic research. It is the first time that scientists have been able to pinpoint a genetic defect despite two important handicaps: the defective protein in CF had not yet been identified and thus could not help to lead the way to the gene, and the defect itself was a "point" or minute change, rather than a larger scale rearrangement of the genetic material. For this reason, the recent discovery is an important precedent for research on other genetic diseases.

NIDDK grantees Dr. Lap-Chee Tsui at the Hospital for Sick Children in Toronto, Canada and Dr. Francis Collins at the University of Michigan, Ann Arbor, collaborated with colleagues at both institutions to find the CF gene. NIDDK conducts and supports studies on the genetics, disease

process, and therapy of CF, and leads and coordinates the CF research effort at the National Institutes of Health. The National Heart Lung, and Blood Institute, the National Institute of Dental Research, and the National Institute of Allergy and Infectious Diseases also support a significant amount of research on this disorder. The National Institute of General Medical Sciences, the National Institute of Arthritis and Musculoskeltetal Diseases, and the Division of Research Resources also support CF research.

A Picture of The Disease

CF causes chronic and usually lethal lung and digestive disease. CF can mimic other diseases, and its manifestations vary among patients. As a result, CF escaped accurate description until the late 1930's, and the disease can escape prompt diagnosis even today. In the 1940's, scientists recognized that thick and copious mucus secretion in patients with CF was a generalized defect and one that underlies the associated lung and digestive disease. An abnormality in the salt levels in sweat reported in the 1950's became the basis for a test that for decades has been essential to accurate diagnosis. The salt abnormality also proved to be a key to identifying the fundamental genetic defect in CF.

Therapy for CF has been limited to relieving the relentless effects of the disease. The thick mucus in the lungs and pancreas of people with CF results in chronic cough and lung infections and impairs the secretion of pancreatic enzymes needed for digestion. Pulmonary (lung) therapy consists of thumping the chest at various angles to loosen mucus and make it easier to expel. Antibiotics are used to combat lung infections, and enzyme supplements help nutrition. With advances in these therapies since CF was first identified, newborns with CF who would once have died in infancy can now hope to live into their adulthood. Their life expectancy, while improved, is, nonetheless, 50 years shorter than that for a child in normal health.

Families with a CF-affected child have a 25 percent chance that each subsequent child they may have will also have CF. The illness exacts a tremendous emotional and economic toll from these children and their parents. For young adults with CF, the disease can complicate finding a job and obtaining health insurance. CF can also impair an individual's ability to conceive and bear children.

Discovery of The CF Gene

The discovery of the CF gene is an important first step towards changing treatment of CF from palliative therapy of the symptoms to treatment of the cause. For years, CF was the subject of a frustrating search for a fundamental defect that could explain all the manifestations of the disease.

Hypotheses came and went. According to one, CF was a disorder of the metabolism of protein components of mucus. Another held that CF resulted from a factor in blood that affected the action of cilia, the fine hairs that move mucus along lung passages.

Advances in biologic research methods in the 1970's permitted the first breakthrough in CF research in 1983. Dr. Paul Quinton, an NIDDK-supported researcher at the University of California, Riverside, reported reduced permeability to chloride in the secretory ducts of the tissues that line CF-affected glands. Other investigators observed similar ion transport defects in other CF-affected tissues. Continuing work on ion transport defects is a major area of CF research, as described later in this report.

During the 70's and 80's geneticists also made rapid advances in their ability to study and manipulate genes. Because genes serve as blueprints for proteins, the structure of a putative CF gene could be inferred from the structure of an abnormal protein, and conversely, the defective protein could be identified if the gene were isolated. CF has a clear and consistent pattern of inheritance. For that reason, scientists began to look for the CF gene, which would then reveal a protein product that presumably affected ion transport.

But the genetic material in the 23 pairs of chromosomes that constitute the human genome, or genetic information, is vast. The search had to cover the roughly 3 billion base pairs--steps in the ladder-like structure of DNA--and at the beginning, there were no signposts. One of the investigators who identified the gene compared the search to looking for a house somewhere in the United States without having a street address.

The search began in earnest in the early 1980's, after geneticists had developed a method called restriction fragment length polymorphism (RFLP) analysis. This method relies on sites in the chain of genetic material, or DNA, which vary from person to person. The variations, known as markers, may mean nothing as far as health or physical appearance is concerned, but they serve as landmarks for someone seeking a gene with an identifiable function. The closer a marker is to a gene, the more frequently the marker and the gene will be inherited together.

In RFLP analysis, scientists use DNA probes, sequences of DNA that are artificially synthesized or cloned (copied) from an organism's DNA and radioactively labeled to find markers that are linked (close) to a gene.

At first, scientists tested available probes at random to see if they identified DNA variations inherited with the CF

trait. In October of 1985, Dr. Lap-Chee Tsui and colleagues working with Collaborative Research in Boston, Massachusetts, announced the linkage of CF to a marker located on chromosome 7. In so doing, they were able to narrow the search to 1 of the 23 pairs of chromosomes that make up the human genome.

Over the next 4 years, Dr. Tsui's team and scientists at other centers here and in England continued the search. Other markers were identified and collaborative studies supported by NIDDK provided information on the orientation of these markers.

In 1987, Dr. Tsui began collaborating with Dr. Francis Collins at the University of Michigan in Ann Arbor. Dr. Tsui screened many DNA probes at random in order to find markers linked to CF. The locations of these markers on the DNA chain, based on the frequencies with which they were inherited with CF, formed a linkage map from which actual distances could be estimated but not measured physically.

In complementary work, Dr. Collins began assembling a physical map of the DNA in the area of chromosome 7 near the CF gene. Once a marker was identified that was close enough to the gene, the scientists used it as a starting point by finding a segment that overlapped with it. They repeated the process, with each subsequent segment overlapping the last. In this way, the scientists "walked" in short steps, or "jumped" in long steps to the beginning of the gene.

In order to determine whether any of the DNA sequences they found contained the CF gene, the scientists compared these sequences with DNA copied from messenger RNA, a molecule that transmits DNA instructions to the cellular machinery. Collaborating scientists had made copies of messenger RNA found in sweat gland tissue, an example of the tissue type affected by CF.

The gene they found is about 250,000 base pairs long. It encodes a protein that appears to play a role in regulating ion transport across cell membranes, a property that is consistent with ongoing research on the fundamental defect in CF. About 70 percent of the people who have CF have a mutation in which 3 of the 250,000 base pairs in the gene are missing. This deletion results in production of a protein that is missing one amino acid of the thousands that serve as the building blocks of the protein.

Now that the gene has been identified, research will progress on a number of fronts. The precise function of the protein encoded by the CF gene must be determined. This will shed light on how the abnormal protein causes lung and digestive disease and may allow development of drugs tailored to correct the defect. Different families with CF will be studied to see if variations in the genetic defect can account

for the variable severity and manifestations of CF among families.

The identification of the CF gene should allow improved screening for this disorder so that patients can be promptly diagnosed and treated. Ultimately, finding the gene lays the groundwork for research on methods of genetic therapy to correct the gene that causes CF and thus to prevent or cure the disease.

Chloride Channels in CF

It is known that the CF defect lies in regulation of chloride channels rather than in the structure of the channels themselves. Regulation of these channels is more complex than thought. Last year, scientists reported that chloride channels in normal cells were activated by an enzyme that catalyzes the addition of phosphate to proteins. (The addition of phosphate to target proteins, a process called phosphorylation, is an important regulatory mechanism in biologic processes.) In CF, this enzyme does not activate chloride channels.

This year, two teams of NIDDK-supported scientists found that a second phosphorylating enzyme, protein kinase C, is also capable of regulating chloride channels, and that this regulatory action is altered in cells from CF-affected patients. Dr. Carole Liedtke and colleagues at the NIDDK-supported CF research center at Case Western Reserve University in Cleveland, Ohio, and other scientists and another team including NIDDK grantee Dr. Dieter Gruenert at the University of California, San Francisco, made similar observations of the ability of these two kinases (phosphate-adding enzymes) to regulate chloride channels. Both teams suggest that the defect identified in the CF gene may affect chloride transport by altering the target site on which the two enzymes normally act. Studies of these enzymes and how they interact with and control chloride channels will shed light on how chloride transport is impaired in CF.

The channels through which chloride is transported across membranes are proteins that help form the structure of the cell membrane. Last year, two teams isolated and then reconstituted chloride channels. Dr. Quais Al-Awqati, director of the NIDDK-supported CF research center at the Columbia College of Physicians and Surgeons in New York, and his colleagues, and another team of scientists including grantee Dr. William Dubinsky at the Baylor College of Medicine in Houston, in collaboration with the NIDDK-supported CF research center at the University of Alabama, purified

chloride transporter proteins and then reconstituted them in membranes that mimic the structure of the cell membrane. In this manner the structure and ion-transporting function of these proteins and their relationship to the protein encoded by the defective CF gene can be studied in detail.

Cell Culture Enhances Supply of Tissue for CF Research

One requirement for CF studies is the availability of tissues that are affected by CF. Normal cells will live and grow in culture for only a limited amount of time. For this reason, research on aspects of physiology that are altered in CF, such as mucus secretion, has been limited to what can be performed with the supply of tissues from CF patients available at autopsy.

Dr. Dieter Gruenert of the University of California, San Francisco, and colleagues, collaborating with scientists at the University of Iowa, have developed cultures of cells that line the surfaces of the trachea. These normal cells are known to be affected by CF. The scientists treated the cells from patients with and without CF with a virus that "transforms" them into cells that will grow indefinitely. The cells retain the traits that are characteristic of them *in vivo* (in the body), and the chloride channels in these cultured cells also have properties similar to those of intact tissues.

Cultures of cells that will survive indefinitely in the laboratory are invaluable to the study of the mechanisms that are altered in CF. They will, for example, be useful in testing how the secretory functions of these cells are affected by the protein made by the CF gene. Ultimately, they may be used to test drugs or other treatment approaches to correct the defective chloride transport in CF.

National Heart, Lung, and Blood Institute

Research on cystic fibrosis supported by the National Heart, Lung, and Blood Institute (NHLBI) focuses on the diseases manifestations in the lungs.

Techniques Developed to Produce "Immortalized" Cells for CF Research

As noted earlier, research on the genetic and biochemical abnormalities underlying CF-associated lung problems has been hampered by limited availability of cells and tissues from the airways and lungs of CF patients. This difficulty, however, may be alleviated by recent advances in the culture and transformation of human airway epithelial cells.

Dr. James R. Yankaskas, a grantee at the University of North Carolina, Chapel Hill, has used gene transfer techniques to produce several CF cell lines that grow indefinitely. His method involves incorporation of the desired genetic package into a retrovirus (a virus whose genetic code is contained in ribonuclaic acid (RNA) rather than DNA like other viruses) that is used subsequently to "infect" airway epithelial (lining) cells. One of these cell lines faithfully expresses what appears to be a fundamental abnormality of airway epithelium in CF: increased transport of sodium ions across the cell membrane but relatively impervious to the transport of chloride ions.

Chloride Ion Transport Defect in Airway Epithelia Explored

Abnormal electrolyte (ion) transport by epithelia is the best characterized cell defect in CF. Much of the work on it has been driven by two observations: 1) multiple CF epithelia including airway, intestinal and sweat duct epithelia and probably pancreatic epithelia, are impermeable to the chloride ion; and 2) the rate of sodium absorption is increased in CF airway epithelia.

Dr. Michael J. Welsh, a grantee at the University of Iowa, Iowa City, is studying the defect in chloride ion transport in airway epithelia. This defect has been localized to an abnormality in the membrane chloride ion channels which are present in the membranes of CF cells but fail to open in response to hormones and neurotransmitters that normally stimulate chloride ion secretion. The failure of CF chloride ion channels to open suggests a defect either in the channel or in an associated regulatory protein.

In studies on another mechanism of chloride ion channel activation, Dr. Welsh has observed that activation of the chloride ion channel in the intact cell can be obtained by addition of a calcium ionophore, a compound that increases the permeability of the cell membrane to calcium. He has found that calcium-dependent regulation of the chloride ion channel in the CF cell is the same as in the normal cell, raising the possibility that this pathway could be exploited to increase chloride ion transport in CF airways.

National Institute of Dental Research

The National Institute of Dental Research (NIDR) supports research relevant to cystic fibrosis primarily through studies of saliva and salivary glands. In CF patients saliva often becomes abnormally thick and sticky and can block salivary ducts, making them susceptible to infection that can spread throughout the body. CF patients also may have difficulty in speaking and swallowing. By uncovering normal mechanisms of salivary secretion, NIDR investigators hope to determine what causes abnormal secretions such as those in patients with CF.

Researchers Elucidate Ion Transport Mechanisms

Much of NIDR-supported research related to CF focuses on the faulty ion transport in salivary epithelial cells, (the component cells in salivary and sweat glands, among others).

Over the past 2 years, NIDR intramural scientists Drs. R. James Turner, Michel Manganel, and James Melvin have studied major membrane transport systems involved in the secretion of saliva. Using acinar cells, sac-like salivary cells, removed from the rat parotid gland, an excellent model of the human parotid and one of three major pairs of salivary glands, these investigators discovered a sodium proton exchanger protein activated by nerves that release the neurotransmitter acetylcholine. They also found that calcium governs the activity of this transport protein. In addition, they uncovered a protein that exchanges bicarbonate ions from inside acinar cells for chloride ions outside these cells. This finding reveals a new pathway for chloride to enter acini and, because chloride drives salivary fluid secretion, to affect the secretion of saliva.

In related studies, these researchers showed that bicarbonate can play a role in saliva secretion by substituting for chloride ions leaving acinar cells. These studies suggest that, in the absence of adequate chloride movement, bicarbonate transport can sustain salivary fluid secretion at low levels.

Continued work on ion transport has led to partial purification of a membrane protein in the rabbit parotid that provides the main "driving force" for salivary secretion by driving chloride into the cell. Understanding these transporter mechanisms may aid in developing therapy to bypass the secretory defect.

Calcium Mediator Proteins Are Identified

For the past 2 years, an NIDR grantee, Dr. John R. Dedman of the University of Texas Medical School, Houston, has worked on identifying proteins that regulate calcium levels in cells. One of these proteins, because of its location in epithelial

cells, which may be related to the physiological defect in fluid secretion in patients with CF. Tissue studies in rats have been complemented by bovine studies in which the calcium mediator proteins that have been identified are used to study differences in chloride outflow from cell compartments. The goal of these studies is to develop a pharmacological agent to "turn on" a defective calcium-regulating chloride channel.

Advances Are Made in Understanding Normal Salivary Secretion

Intramural investigators Drs. Bruce Baum, Indu Ambudkar, and Valerie Horn have further elucidated the complicated cascade of events involved in normal saliva secretion. They discovered that adrenaline, which is closely related to noradrenaline, a neurotransmitter released by nerves in salivary glands, uses a combination of cellular signals to elicit secretory events. Most notably, they showed that a mediator compound called cyclic adenosine monophosphate (cAMP) can increase the amount of free calcium in salivary acinar cells. Increased calcium heightens chloride transport and associated saliva secretion.

The findings show that the two main signal pathways in these epithelial cells are interrelated. This is important because it is believed that cAMP-mediated actions are flawed in CF patients. The investigators also have characterized the key transport protein that controls calcium movement out of parotid acinar cells, the adenosine triphosphate (ATP)-dependent calcium pump.

Recently, these same investigators have found that, when parotid cells are stimulated simultaneously with more than one neurotransmitter, there is a negative regulation in the generation of signals inside the cell which, in turn, limits the cell's response. This finding is physiologically important because a cell is usually challenged by more than one neurotransmitter at a time. Regulation is believed to occur at the level of signal generation, which involves a receptor signalling protein, G protein, and an intracellular effector enzyme involved in generating the signal. The researchers are following up on these findings to elucidate the molecular mechanism involved in this regulation.

Using normal cells removed from another, quite different, rat salivary gland--the submandibular gland--NIDR grantee Dr. Thomas Hurley of the University of Missouri in Columbia has quantified the changes in cellular calcium that occur in response to various types of nerve stimulation. In related work, he has found abnormalities in the ATP-dependent calcium pump in submandibular and pancreatic cells removed from a rat model of CF. Dr. Hurley found that the amount of this transporter is greatly reduced in these cells in comparison to that found in normal cells. This reduction would likely hamper the abilities of salivary cells to control calcium

balance and thus secrete saliva and of pancreatic cells to secrete digestive enzymes. Both abnormalities are characteristic of CF.

All these findings suggest steps in the pathway of epithelial gland secretion that might be deranged in CF. Elucidation of these faulty steps will lead to more targeted approaches for treating CF patients.

National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases (NIAID) supports research on the mechanisms by which infectious organisms cause diseases in humans and uses this knowledge to develop improved therapies and vaccines to prevent these diseases.

Bacterial Peptide to Serve as Basis for Vaccine

Infection with the bacterium Pseudomonas aeruginosa is common and often life-threatening in people who have cystic fibrosis. Scientists have learned that this bacterium produces a variety of chemicals harmful to the body, the most toxic of which is a protein called exotoxin A (ETA). Experiments in both animals and humans have suggested that vaccines against ETA may help control pseudomonas infections in people who have CF.

At Harvard University in Cambridge, Massachusetts, NIAID grantee Dr. Robert Collier has used recombinant DNA technology to identify the position of a critical amino acid, glutamic acid, in the ETA molecule, which makes it toxic. Using a technique called site-directed mutagenesis, Dr. Collier deleted the amino acid and replaced it with harmless ones.

Because the altered ETA molecule is nontoxic and stable, but still retains its ability to stimulate an immune system response, investigators have used the altered ETA as the basis of an anti-pseudomonas vaccine. Plans are underway to begin Phase I clinical trials of this vaccine to test its safety and ability to stimulate the immune system. In addition, the scientists will try to combine the altered ETA with other components of P. aeruginosa that also play a role in stimulating immunity, in order to develop the most effective vaccine possible.

Division of Research Resources

The Division of Research Resources (DRR) supports and conducts research into cystic fibrosis at shared research facilities across the United States. About half of CF patients die by age 25, their lungs damaged by infection and hampered by mucus. But DRR grantee Dr. Michael Knowles and his associates at the North Carolina School of Medicine General Clinical Research Center (GCRC) in Chapel Hill, and the Duke University GCRC in Durham, North Carolina, are studying a CF family whose members have lived twice as long with much less severe symptoms than most CF patients. Understanding this milder type of CF may lead to the discovery of new ways to diagnose the disease and treat its severest forms, according to the grantees.

GCRC's provide the research infrastructure for multidisciplinary studies on both children and adults. Specifically, they provide patient research facilities, computerized data management and analysis, as well as research nurses, dietitians, biostatisticians, and specialized laboratories for the translation of basic and clinical research into medical practice.

The scientists found that the older CF patients in the family with milder disease produced normal amounts of the pancreatic enzymes needed to digest food. Also, their lung infections are less destructive than those in patients with typical, more severe CF. Two family members have reached the ages of 52 and 62 years, more than double the life expectancy for patients with severe CF.

Family members who married relatives bore offspring with especially mild symptoms, indicating that the milder form of the disease could be linked to a unique genetic mutation. Uncovering this mutation could lead to the development of tests to accurately identify all CF carriers, who constitute about 5 percent of all Caucasians. Dr. Knowles hypothesizes that the research may even help bring about a treatment that could modify the severe form of CF to a milder form of the disease.

Lung failure is the cause of premature death among most patients with CF. As a result, these patients increasingly are undergoing heart-lung transplantation from a normal donor and simultaneously donating their normal hearts for transplantation into other patients. By combining these procedures, two patients are helped and the surgery on the CF patient is simplified. Because patients receiving these transplants are at risk of rejecting the organs, drugs must be administered to suppress the immune response.

CF patients have trouble absorbing some foods and drugs. Therefore, DRR grantee Dr. Gerard Cooney at Temple University

School of Pharmacy and his associates at the Temple University GCRC in Philadelphia, Pennsylvania, have been investigating the absorption by these patients of cyclosporine A, one of the most effective drugs for suppressing the immune systems of transplant recipients. The grantees studied six CF patients who were awaiting heart-lung transplantation and two healthy individuals. Each received oral doses of cyclosporine A. Blood samples were drawn during the following 24 hours. The next day the drug was administered intravenously with blood samples again drawn over the following 24 hours. Some subjects also received a special enzyme supplement designed to promote absorption of the drug from the gastrointestinal tract.

Dr. Cooney and his colleagues found that the healthy individuals absorbed cyclosporine A at twice the rate of CF patients, even when the CF patients received enzyme supplements. The grantees concluded that CF patients may require two to four times the usual dose of cyclosporine A to achieve adequate levels of the drug.

Outlook

The availability of the CF gene offers hope that, within the lifetime of people now affected by CF, a treatment may be developed that will do more than forestall the effects of this disease for a few years. In the meantime, research by NIDDK and other NIH institutes on aspects of CF such as the function of affected tissues, the mechanisms of secretion, and bacterial lung infections and inflammation remains important to an understanding of CF and to therapy of affected children. Because no one can predict when knowledge of the gene will yield a revolutionary treatment, it is as important as ever to continue other research that will help children and young adults with CF remain as healthy as possible.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

DAY CARE

DAY CARE

Appropriations
(in millions)

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
Office of Human Development Services (Total).....	636.6	671.4	674.2	662.5	675.5
o Social Services Block Grant (Title XX) 1/	630.0	660.0	660.0	660.0	660.0
o Child Welfare Services 2/	n/a	n/a	n/a	n/a	n/a
o Dependent Care Planning and Development	4.8	8.3	11.9	13.2	13.2
o Child Development Associate Scholarships	-	1.4	1.5	1.5	1.5
o Research and Demonstration	1.8	1.7	.8	.8	.8
o Head Start 3/	(1131.5)	(1206.3)	(1235.0)	(1386.3)	(1886.3)
Family Support Administration (Total).....	39.0	40.0	53.0	255.0	539.0
o AFDC Dependent Care Disregard 4/	39.0	40.0	41.0	49.0	50.0
o Child Care during JOBS 5/	-	-	17.0	161.0	322.0
o Extended Child Care Eligibility 5/	-	-	-	32.0	154.0
o Child Care Grants to States 5/	-	-	-	13.0	13.0
o Community Services Block Grant 6/	n/a	n/a	n/a	n/a	n/a
Public Health Service - Research and Demonstration..	2.0	2.5	3.9	4.2	5.0
Assistant Secretary for Planning and Evaluation - Research and Evaluation.....	.3	.7	.6	.9	.4
HHS TOTAL	677.9	714.6	736.7	922.6	1,219.9

(DAY CARE TABLE FOOTNOTES)

1/ Estimates based upon HHS-sponsored research have been used for the cost of day care services which States may choose to provide under the Social Security Act's Title XX formula grants program.

2/ Title IV-B of the Social Security Act establishes matching grants to States who may provide child day care and assist child care centers in meeting licensing requirements, but no cost estimates are available.

3/ Data for the Head Start program are listed for information, but have not been included in totals for the Office of Human Development Services or the Department because Head Start is a comprehensive child development program rather than a child care program.

4/ The AFDC child care disregard can only be estimated because no actual data is submitted by States to the Federal government. No estimate was included of the AFDC Special Needs Allowance which may be attributable to day care or the portion of Community Services Block Grant funds which States allocate to child care.

5/ This provision was added by the Family Support Act of 1988.

6/ The Community Services Block Grant provides grants to States to go to local community action agencies for local antipoverty activities, which may include child care. No data on such expenditures is provided to the Federal government.

OFFICE OF HUMAN DEVELOPMENT SERVICES

Day Care Activities

Social Services Block Grant

- In fiscal year 1988, the last year for which information is available, all States except California and Montana reported that they provided day care services under the Social Services Block Grant (Title XX of the Social Security Act), a $2.7 billion formula grant program ($2.8 billion beginning in fiscal year 1990). Child care services must comply with applicable State and local law. Estimates of State expenditures of Title XX funds for day care are based upon HHS-sponsored research.

Child Welfare Services

- Title IV-B of the Social Security Act establishes 75 percent matching grants to the States. States may provide child day care and may also assist child care centers in meeting State and local licensing requirements. No capital costs for child care facilities may be paid and each State's spending for child care services necessary solely for employment or training is limited to that available in fiscal year 1979. There is no State reporting on the portion of IV-B funds which are expended related to child day care.

Dependent Care Planning and Development

- The Dependent Care Planning and Development program was authorized in 1984. Grants to States pay 75 percent of the planning and development costs to establish information and referral systems and school-age day care. Grants may not be used for operating or capital costs, nor for direct payments or services to beneficiaries.

Child Development Associate Scholarship Program

- The Child Development Associate Scholarship Program began in 1987. States and areas receiving grants under the Social Services Block Grant are eligible to apply for grants, which are distributed in the form of scholarships to those candidates for the child development associate credential whose income does not exceed Federal poverty guidelines.

Other Research

- A range of research on day care has been conducted and is planned by the Office of Human Development Services (HDS). For example, the National Center on Child Abuse and Neglect has funded projects to develop training materials for caregivers on child sexual abuse and child molestation prevention. From 1985 through 1988 numerous projects were funded studying child abuse in out-of-home settings, including assessments of the impact of sexual abuse in child day care settings. Under an HDS partnership with the National Academy of Sciences, a multi-disciplinary Panel on Child Care Policy is examining the state-of-the-art on child care and will recommend child care options along with their associated costs, with results due early in 1990. Additionally, the National Association for the Education of Young Children is conducting a National Child Care Study which will be completed in 1991.

FAMILY SUPPORT ADMINISTRATION

Day Care Expenditures

- AFDC recipients and applicants who need child care in order to work may have the cost they pay for such care subtracted from their earnings in determining their eligibility and benefits. In fiscal year 1990, the Family Support Act of 1988 raised the ceiling of deductible care expenses for each child from $160 per month to $175 ($200 for children under 2). The Family Support Act of 1988 also extends child care eligibility for up to twelve months to the extent that such care is determined by the State agency to be necessary for an individual's employment in any case where a family has ceased to receive AFDC as a result of employment. There are no Federal requirements for facilities or caregivers and States are not required to report separately on the amount of income disregards attributable to child care expenses.

  With HHS approval, there were seventeen States in fiscal year 1988 that adjusted AFDC grants in recognition of the special needs of welfare recipients for child care necessary for certain education or job-related training. Ceilings on costs vary from State to State, but are sometimes the same as the ceilings on child care disregards from the earnings for full- and part-time workers. No estimates are provided on these costs for prior fiscal years. However, the Family Support Act of 1988 established the Job Opportunities and Basic Skills Training Program, which includes child care. Estimates have been provided for fiscal years 1990 and 1991.

- The Family Support Act of 1988 established a program of grants to States to improve their child care licensing and registration requirements and procedures and to monitor child care provided to children receiving aid.

- The Community Services Block Grant provides grants to States to go to local community action agencies for local antipoverty activities, which may include child care. No data on such expenditures is provided to the Federal government.

PUBLIC HEALTH SERVICE

Day Care Research and Demonstration

- The National Institute of Child Health and Human Development has developed a new focus concerning the impact of care environments on child development. The "National Study of Young Children's Lives" is a multi-site, longitudinal, prospective study of the interactive influence of the characteristics of a child and the characteristics of the physical and human environment in which the child resides. Alternative care settings are considered as part of the human and physical environment in which many children find themselves today. The study involves a cooperative agreement between the Institute's Human Learning and Behavior Branch and ten centers across the country.

- The Bureau of Maternal and Child Health and Resources Development also funds a number of projects addressing health and safety problems associated with day care. A current project being conducted through the American Public Health Association and the American Academy of Pediatrics involves a national survey of existing State regulations related to out-of-home child care and a survey to identify exemplary child care programs considered worthy of replication. The project will have developed model health and safety standards in child care settings by the summer of 1990. Other projects will demonstrate how child care provider training and implementation of personal hygiene and environmental sanitation in day care can reduce transmission of infectious diseases, how health status is related to the type of care selected by the parent, and how to develop a pediatric extended day care facility for medically compromised children and their families.

ASSISTANT SECRETARY FOR PLANNING AND EVALUATION

Child Care Research and Evaluation

The Family Support Act of 1988 instituted a job opportunity and basic skills (JOBS) program which requires AFDC recipients to engage in education, employment, or job training as a condition for receiving AFDC benefits.

The Assistant Secretary for Planning and Evaluation (ASPE) has responsibility for evaluating the JOBS program. Part of this evaluation will examine the effects of parents' participation in JOBS on their children's development. The evaluation contractor, MDRC, has subcontracted with ChildTrends Inc. to produce research design options outlining the effect of participation, controlling for family variables and alternative care arrangements, on children's social, emotional, cognitive, and physical development.

In addition, ASPE has contracted to explore the effect of JOBS' transitional child care and Medicaid benefits on parents' short- and long-term self-sufficiency.

ASPE is also helping to fund major surveys of child care. ASPE has an interagency agreement with ACYF to conduct a National Child Care Consumer Survey, which will provide a nationally representative picture of how children are being cared for. It will obtain information on preferences for and use of various child care arrangements among both employed and non-employed mothers.

ASPE also plans to help fund an intensive longitudinal study of the effect of alternative care arrangements and family environment on infants' development. National Institute of Child Health and Human Development's Infant Care Network is following 1200 families with infants in ten sites for three years, documenting infants' developmental milestones, and will assess the effects of child care variables and family functioning variables on the outcomes.

Finally, responding to both concerns about the unavailability of quality infant care and the effects of early, extensive nonparental child care, ASPE is working to improve the knowledge base of infant attachment theories by holding a research seminar. Seminar participants will be noted researchers in infant attachment theory from a variety of psychodynamic disciplines and will produce a literature review and recommend a research agenda for policy relevant analyses.

DIABETES AND RELATED RESEARCH
Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
National Institutes of Health:					
National Institute of Diabetes and Digestive and Kidney Diseases	$141,089,000	$146,988,000	$147,050,000	$150,000,000	$157,700,000
National Cancer Institute	965,000	819,000	929,000	960,000	1,004,000
National Heart, Lung and Blood Institute	14,793,000	15,109,000	16,101,000	16,500,000	17,150,000
National Institute of Dental Research	3,489,000	3,010,000	4,318,000	4,473,000	4,639,000
National Institute of Neurological Disorders and Stroke	8,876,000	7,995,000	9,383,000	9,682,000	10,107,000
National Institute of Allergy and Infectious Diseases	5,764,000	6,553,000	5,336,000	5,656,000	5,895,000
National Institute of General Medical Sciences	2,432,000	2,585,000	2,668,000	2,700,000	2,700,000
National Institute of Child Health and Human Development	12,432,000	12,168,000	13,343,000	14,000,000	14,600,000
National Eye Institute	21,751,000	22,050,000	21,086,000	21,405,000	22,548,000
National Institute of Environmental Health Sciences	203,000	178,000	196,000	203,000	211,000
National Institute on Aging	3,808,000	4,772,000	4,805,000	4,973,000	5,170,000
Division of Research Resources 1/	17,516,000	16,771,000	17,432,000	17,215,000	17,466,000
National Center for Nursing Research	524,000	1,515,000	1,324,000	1,500,000	1,500,000
Office of the Director 2/	510,000	369,000	753,000	925,000	502,000
Total, NIH	234,152,000	240,882,000	244,724,000	250,192,000	261,192,000

DIABETES AND RELATED RESEARCH - continued
Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
Centers for Disease Control.....	7,100,000	10,113,000	10,625,000	10,651,000	10,679,000
Alcohol, Drug Abuse, and Mental Health Administration.....	---3/	300,0003/	613,000	613,000	613,000
Indian Health Service.....	---3/	2,900,0003/	3,900,000	5,400,000	5,400,000
Total, PHS....	241,252,000	254,195,000	259,862,000	266,856,000	277,864,000

1/ This includes RCMI awards. Prior to FY 89, RCMI's were shown in OD.

2/ This includes AREA awards for FY 1987 - 1991, and RCMI awards for FY 1987 and 1988.

3/ Previously unreported: Alcohol, Drug Abuse, and Mental Health Administration 1987 - $303,000; IHS 1986 - $1,900,000; and 1987 - $2,900,000.

NATIONAL INSTITUTES OF HEALTH

National Institute of Diabetes and
Digestive and Kidney Diseases

DIABETES

An estimated 11 million Americans have diabetes. Almost twice that many have a condition that is both a risk factor and a precursor to diabetes--impaired glucose tolerance (IGT). In both diabetes and IGT the body does not respond adequately to the presence of the sugar glucose in blood. People with diabetes, half of whom don't know they have the disease, are at risk for complications that include heart, eye, nerve, and kidney disease. Even those with IGT have a higher than normal risk of high blood pressure, heart disease, and stroke, and many of these people go on to develop full-blown diabetes.

Research on how glucose metabolism becomes abnormal in people who have IGT and diabetes is revealing the intricate mechanisms by which glucose is transformed into energy. Research is also showing how interventions can be designed to prevent diabetes and its complications and reduce the physical and emotional hardship and the economic loss this disease causes each year. The medical expenses and lost income from the complications of diabetes cost the country an estimated $20.4 billion annually.

The Disease

People with diabetes have difficulty using glucose for energy. Glucose is a product of the breakdown of starches and more complex sugars during digestion. Once glucose enters the bloodstream, insulin, a hormone produced by the pancreas gland just behind the stomach, regulates the use of glucose by muscles, liver, and fat tissue.

Ninety-five percent of Americans with diabetes have what is called noninsulin-dependent diabetes (NIDDM). Two defects combine to cause it. One defect is that the target tissues of glucose--such as the liver and muscles, which normally use glucose for energy or to store energy--become unresponsive to insulin. If the pancreas can make enough insulin to overcome this insulin resistance, then blood levels of glucose remain normal. If a defect in insulin secretion prevents the pancreas from keeping up with insulin production, however, blood glucose begins to rise. Detection of this elevated blood glucose is the basis of the diagnosis of diabetes and IGT.

Research is showing that the relationship between these two defects is more complex than once expected. For example, insulin treatment can improve the ability of target tissues to

respond to insulin and actually lower requirements for it. Also it is likely that many different molecular errors can cause the insulin resistance of NIDDM. Molecular-level studies of how insulin is secreted and how it acts also are revealing many points in the process where abnormalities can set the stage for illness.

Approximately 5 percent of Americans with diabetes have insulin-dependent diabetes (IDDM), which results from failure of the pancreas to produce insulin. IDDM is an autoimmune disease, in which the body's immune, or disease-fighting, system turns against itself and destroys insulin-producing cells. Unlike NIDDM, which usually begins in adulthood, IDDM usually begins in childhood. Without insulin replacement, IDDM is rapidly fatal.

Effective treatment exists for both forms of diabetes. NIDDM can usually be treated with diet and exercise. Oral drugs and insulin can be used if diet fails to control the disease. Daily insulin injections and a careful diet are a necessity for people with IDDM. For both kinds of diabetes, however, careful treatment does not eliminate the possibility of complications such as heart and kidney disease. Even with careful treatment, complications become more likely after many years of having diabetes.

The complications of diabetes are widespread and severe. About half of the approximately 100,000 lower extremity amputations performed each year in the United States are on people with diabetes. Diabetes-associated nerve disease (neuropathy) impairs sensation and healing in the legs and feet, and leads to infections, gangrene, and ultimately amputation. Diabetes accounts for almost one-third of new cases of end-stage renal disease in this country. Death from kidney disease is 500 times more common among young adults with IDDM than in the general population.

As the leading cause of new blindness in adults, diabetes causes approximately 5,800 people to become blind each year. Babies of diabetic mothers are five times more likely to require intensive perinatal care than are babies born to women without diabetes.

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and many other institutes at NIH conduct research aimed at increasing our understanding of diabetes and providing the means to prevent this disease and its complications. Among the advances scientists have reported this year are an experimental treatment of IDDM based on current understanding of the immunology of the disease; clinical trials of a new insulin pump that is completely implantable and uses technology from the space program; and a number of discoveries that will enhance our understanding of the molecular biology of diabetes.

The NIDDK leads and coordinates NIH-sponsored research on diabetes. In addition to the contributors to this report, the National Institute of Environmental Health Sciences and the NIH Office of the Director also support diabetes research.

Immunology and IDDM

A clinical trial in Florida is a good example of how research on the underlying mechanism of a disease like diabetes can lead to the development of new treatments. NIDDK grantees Drs. Janet Silverstein and Noel Maclaren and their colleagues at the University of Florida, Gainesville, are among the research groups who have tested the effects of giving immune-suppressing drugs to people with newly diagnosed IDDM in hopes that the drugs would slow or stop islet cell destruction by the immune system. Dr. Silverstein's group randomly assigned 46 patients with IDDM to either immunosuppression or to a control group with no immunosuppression. In half of the 20 patients who received immunosuppression, the treatment reduced the amount of insulin they needed to keep their diabetes under control. Three of these patients, compared with none of the controls, needed no insulin after a year.

These results provide a clue as to how IDDM might one day be prevented. Hurdles that must still be overcome are the side-effects of the drugs, which include nausea, reduced immunity to infection, and a long-term risk of cancer. In some patients, the beneficial effects of the drugs wear off: in the University of Florida trial, four of the patients who at first responded well to treatment eventually stopped responding. In all of the patients, immunosuppressive treatment must continue indefinitely to maintain the benefits of the drugs, so the risk of side effects must be balanced against the long-term hardship and hazards of diabetes.

Other lines of research are providing information about how the immune system destroys pancreatic islet cells. Dr. Kevin Lafferty and colleagues at the University of Colorado at Denver have isolated and cloned several lines of immune cells, called T lymphocytes, that induce destruction of islet cells. When these T cells were transplanted along with pancreatic islet tissue, which was then transplanted into mice, the transplanted tissue was destroyed by the host. Islet tissue transplanted without the T lymphocytes survived in the host. Continuing research will seek to identify the antigen target attacked by these T lymphocytes and to determine what sets these cells on a destructive course and how they destroy islet tissue. With information on this process, scientists may be able to design ways to intervene, perhaps by developing ways to destroy or block the T lymphocytes while sparing the rest of the immune system.

NIDDM and Insulin Secretion and Action

In NIDDM, both the secretion of insulin and the body's response to it are abnormal. Dr. Kenneth Polonsky and colleagues at the University of Chicago in Illinois have found that, in people with normal glucose metabolism, insulin is secreted in pulses about 90 to 120 minutes apart. The height of the pulses--reflecting how much insulin was secreted--but not the frequency, of the pulses increases with meals. In the obese, who have a higher than normal risk of developing diabetes, the mealtime pulses are higher than in average-weight people, but otherwise the secretion pattern is similar. The researchers found that people with NIDDM produce about the same amounts of insulin over 24 hours as those without NIDDM, but the timing of the insulin pulses is altered.

The pancreatic islets secrete other glucose-regulating hormones in addition to insulin. Glucagon is another example of an islet hormone that affects blood glucose levels. Dr. Donald Steiner and colleagues at the University of Chicago have isolated the human gene for amylin, a protein that accumulates in the islet cells of people with NIDDM. Dr. Steiner's group has found that the protein, like other protein hormones, including insulin, is made from a large precursor molecule. Dr. Christopher Newgard and colleagues at the University of Texas Southwestern Medical Center in Dallas have cloned the rat amylin gene and have shown that this gene is expressed--that is, it is translated into a specific protein for which it serves as a blueprint--only in pancreatic islet cells. These studies indicate that amylin may be another hormone that, like insulin, plays a role in the development of diabetes.

Studies of hormone production and secretion are helping scientists understand the nature of the pancreatic defect in NIDDM. The information gained may provide clues to modulating insulin secretion and to replacing insulin or other hormones that affect blood levels of glucose.

After it is secreted by the pancreas, insulin binds to receptors on the surfaces of cells. Binding of the hormone to the receptor sets off a cascade of steps that results in the use of glucose by the cell. The insulin receptor and its function are primary interests of scientists in NIDDK intramural laboratories. Dr. Simeon Taylor and colleagues at NIDDK have been studying patients with rare inherited syndromes characterized by extreme resistance to insulin. Though rare, these syndromes provide an opportunity to identify biochemical defects leading to insulin resistance. Last year, for example, the NIDDK scientists identified mutations or changes in the genetic information for the insulin receptor in a patient with extreme insulin resistance. One mutation affected the receptor's

incorporation into the cell surface, while the other mutation resulted in a truncated receptor.

This year, the same team identified a third type of mutation in the insulin receptor gene of a patient with extreme insulin resistance. This mutation resulted in the switch of 1 of the 1,370 amino acids that make up the insulin receptor protein. The substitution is at an important location for the receptor. The change disrupts the receptor's ability to phosphorylate, or add phosphate to, proteins. Phosphorylation is an important switching mechanism in biologic systems, and is thought to be necessary for the insulin receptor to set off the essential changes in the cell for glucose metabolism. This work confirms the importance of the insulin receptor's kinase (phosphate-adding) activity and illustrates how a defect in one of many critical steps leading to glucose use can result in illness. Mutations such as this one are likely to play a role in the more common form of NIDDM.

One of the processes set off by the binding of insulin to its receptor is the "recruitment" within the cell of molecules that can transport glucose. Several different NIDDK-supported groups have identified different glucose transporter molecules. Dr. Morris Birnbaum and colleagues at Harvard University in Boston, Massachusetts; the VA Medical Center in San Diego, California; and the Indiana University School of Medicine, Indianapolis, examined what happened to the production of glucose transporters in diabetic mice before and after treatment with insulin. The glucose transporters this group studied were cloned from tissues known to be responsive to insulin: skeletal muscle and brain.

The scientists measured the amount of messenger RNA (mRNA)--a form of genetic material that transmits inherited information from the cell nucleus to the cell's protein-making machinery--in diabetic rats and in rats treated with insulin. In muscle and fat tissue, both of which are target tissues for insulin, the amount of mRNA coding for a glucose transporter was greatly reduced in the diabetic rats, but was restored after insulin treatment. This glucose transporter was originally isolated from skeletal muscle tissue. These findings indicate that changes in this transporter may account for much of the insulin resistance seen in these diabetic animals.

This research is helping scientists understand the origins of insulin resistance and the reasons that insulin resistance in patients with NIDDM seems to be both a cause and a consequence of diabetes. It also demonstrates how insulin treatment can improve diabetes, not only by bringing blood glucose to a normal level, but by improving the body's metabolic response to glucose.

Insulin Delivery

Replacement of insulin is life saving in people with IDDM. Insulin also plays an important role in the treatment of NIDDM. Insulin replacement does not provide a perfect solution to diabetes, however. Even with daily injections and blood glucose monitoring, people with diabetes are still at risk for developing the long-term complications of diabetes. Self-administered injections are uncomfortable, and logistical concerns can be disruptive. Making sure to have the correct supplies and taking the time to give injections at the appropriate times each day are burdensome requirements of therapy. These are some of the reasons researchers have sought improved means of administering insulin. Scientists are attempting to develop methods of insulin administration that mimic the ways the body normally delivers the hormone. Studies are also examining whether insulin administered in this manner could reduce the risk of complications.

This year, scientists reported on clinical tests of an implantable insulin pump developed and tested with NIDDK support. Robert Fischell of the Johns Hopkins University Applied Physics Laboratory, Laurel, Maryland, developed the pump using technology borrowed from the space program. Dr. Christopher Saudek at the Division of Research Resources -supported General Clinical Research Center at Johns Hopkins University School of Medicine in Baltimore, Maryland, collaborating with scientists at the University of California, Irvine, conducted clinical tests of the pump in patients with IDDM.

The pump, called the programmable implantable medication system, or PIMS, measures about 3 inches in diameter, is 3/4 inch thick, and weighs about 8 ounces when filled with insulin. It is implanted in the patient's abdomen. Some of the features the designer of the pump adopted from the space program are the pump's titanium casing, its self-checking systems for ensuring that the pump does not malfunction and dispense too much or too little insulin, its ability to be programmed by a remote transmitter, and its telemetry system with which it can report to the physician's computer how much insulin has been dispensed hourly for the previous 21 days, or daily for the previous 60 days.

The pumps were implanted in 18 patients with IDDM. The pumps were programmed by an external radio transmitter to deliver a basal rate of insulin in pulses throughout the day, and could be directed by the patient to give mealtime doses as needed. In the 25 months of the study, one pump was replaced because of a failure of a microelectronic chip. Otherwise, the pumps functioned as they were designed. In four patients,

surrounding tissue encapsulated the pumps, interfering with insulin dispensing. Two of these patients withdrew from the study, and two had the pump catheters freed surgically from the encapsulating tissue and continued on the pump.

The pumps helped the patients who stayed in the study to maintain good diabetes control. They had less trouble with fluctuating blood glucose levels than before pump implantation. There were no instances of severe low blood glucose due to insulin overdose, or of dangerously high blood glucose from too little insulin. The scientists concluded that the pump has potential as an alternative means of insulin administration for IDDM. For some patients, PIMS could offer an effective means of taking insulin that is more comfortable than daily injections.

Researchers are trying to develop glucose sensors that may be coupled with such a pump and direct it to deliver insulin as needed based on the glucose level in the body. Such a "closed-loop" system could provide an "artificial pancreas" for an individual whose own pancreas no longer secretes insulin.

National Cancer Institute

This year, the National Cancer Institute contributed to advances in diabetes mellitus research through studies on the growth of new capillary blood vessels, markers for the disease, and on diabetes risk and alcohol consumption.

Dr. Judah Folkman at the Harvard Medical School and Children's Hospital in Boston, Massachusetts; Douglas Hanahan at Cold Spring Harbor Laboratory in Cold Spring Harbor, New York; and colleagues studied genetically engineered (transgenic) mice that carry oncogenes (genes that can cause normal cells to become cancerous) in the beta cells of pancreatic islets. The beta cells of pancreatic islets produce insulin and are the cells attacked and destroyed by the human immune system in development of IDDM. Individuals with diabetes mellitus are at increased risk for development of pancreatic cancer.

The researchers wanted to learn more about the growth of new capillary blood vessels (angiogenesis) in early development of cancer. They did not find angiogenic activity in normal pancreatic islets or early hyperplastic (abnormally proliferating) islets. However, some hyperplastic islets did exhibit angiogenic activity. Data showed that induction of this activity preceded tumor formation and correlated with the transition from hyperplasia to cancer. Hyperplasia itself did not mean that angiogenesis would necessarily occur. The findings suggest that angiogenic capability develops as a result of some change within the hyperplastic islets during the precancerous period.

To conduct the study, the researchers developed an *in vitro* bioassay that detected exactly when the islets switched to an angiogenic state. Together with *in vivo* data from studies in mice, they suggest that the bioassay provides a powerful new method for studying molecular genetic events that govern the induction of angiogenesis and tumor progression.

IDDM has consistently been associated with presence of human leukocyte antigen (HLA) serologic markers HLA-DR3 and HLA-DR4 (HLA markers encoded by the genes in the HLA-D region of the major histocompatibility locus, MHC, play a role in determining the body's immune responses). Focusing on HLA-DR4, Dr. James Rowe at the American Red Cross Blood Services in Madison, Wisconsin, Dr. Edmond Yunis at Dana-Farber Cancer Center in Boston and colleagues in an NCI-supported multi-institutional study investigated its subtypes to look for markers for IDDM. They found that two HLA-DR4 subtypes, Dw4 and Dw10, were associated with IDDM in populations studied in

Boston and Wisconsin. The subtypes did not appear to play a causative role in the disease, however. The researchers suggested that the subtypes may be markers for IDDM in some but not all populations. Associations with different subtypes may be important in other populations.

Researchers from the University of Washington in Seattle and Baylor College of Medicine in Houston, Texas, collaborated on the study. The research was also funded by NIDDK.

Studies have shown both deterioration and improvement in glucose tolerance after alcohol consumption. However, Drs. Meir Stampfer and Frank Speizer at Brigham and Women's Hospital in Boston, Massachusetts, and colleagues found that moderate alcohol intake did not increase the risk of NIDDM. Data were analyzed on 85,000 women who participated in the Nurses' Health Study. The women were 34 to 59 years of age in 1980 and did not have a history of diabetes, coronary heart disease, or cancer. Thirty-two percent of the women were nondrinkers. Of those who drank alcoholic beverages, 79 percent drank less than 15 grams per day (the equivalent of about one-and-one-half glasses of wine per day), and the remainder drank 15 grams.

National Heart, Lung, and Blood Institute

Diabetes research supported by the National Heart, Lung, and Blood Institute (NHLBI) focuses on the disease's role as a risk factor for cardiovascular disease and on its manifestations in the cardiovascular system.

Diabetes Doubles Risk of Recurrent Myocardial Infarction in Women

In people who have recovered from an initial myocardial infarction (MI), standard risk factors, including diabetes, remain important determinants of coronary prognosis over many years. The impact of diabetes on nonfatal recurrent MI and on fatal coronary heart disease was examined among participants in the Framingham Heart Study, an epidemiologic study begun in 1948 to identify risk factors for cardiovascular diseases, estimate the incidence of fatal and nonfatal events related to cardiovascular diseases, and investigate the effects of these diseases. Of the 697 subjects (464 males and 233 females) who experienced an initial MI during 30 years of follow-up in the study, 459 returned for a baseline examination and were followed for up to 32 years (mean: 9.7 years) for reinfarction or coronary death.

In recent analyses, Dr. Philip Wolf, an investigator supported by a contract with Boston University, Massachusetts, found that the risk of nonfatal recurrent MI in diabetic women was twice that in diabetic men. Moreover, the presence of diabetes doubled the risk of recurrent MI in women (relative risk, 2.1) but had an insignificant effect in men. For both sexes, the rate of fatal CHD was significantly greater in diabetic than in nondiabetic individuals. Diabetes increased the risk of fatal CHD by 70 percent among men and by more than 100 percent among women.

Dr. Wolf concluded that a diabetic patient who survives an MI commonly experiences subsequent inability of the heart to maintain adequate blood circulation. When such cardiac failure occurs, control of diabetes assumes added importance, particularly in women, where its effect on recurrent nonfatal MI and on survival is considerable.

Diabetes May Affect Response to Beta-Blocker Drugs

Dr. Frederick S. Fein, a grantee at Yeshiva University, New York City, has studied the effects of beta-blocker drugs on animals with experimental diabetes. Propranolol, a beta-blocker frequently prescribed to human patients with hypertension or heart disease, was administered over several months to normal and diabetic rats. Heart rate decrease was much greater in normal animals than in diabetic animals. The physiologic effects of propranolol in normal animals were as expected, with prolonged contraction times and stronger

pumping action in the heart associated with the fall in heart rate. In contrast, pumping action in the hearts of diabetic rats did not improve. This indication that diabetes may alter cardiac response suggests a need to evaluate the effects of propranolol in diabetic patients with hypertension. The appropriate range of drug doses should be determined for diabetic patients to avoid possible inadequate cardiac output at rest or during stress that may result from less than fully effective pumping action.

Studies on Diabetic Retinopathy Yield Clue to Irreversibility

Diabetic retinopathy involves changes in the permeability of small blood vessels in the retina of the eye, which progress to bleeding and scarring. Progression of early lesions usually continues despite the institution of strict control of glucose metabolism in the patient. In recent studies using human cells grown in culture, Dr. Mara Lorenzi, a grantee at the Eye Research Institute in Boston has shown that exposure to high levels of glucose, characteristic of the diabetic state, results in changes in the activity of certain genes that encode substances forming the matrix in which cells of the retina are embedded. Expression of the genes for collagen, laminin, and fibronectin, three such substances, is increased by exposure to high levels of glucose. A particularly interesting observation with major clinical relevance is that the effects of high glucose are not readily reversible on return to normal concentrations. In this sense, the cells possess a "memory" and continue to behave abnormally even after the stimulus has been removed. This finding is an important early step toward a clearer understanding of the disordered cell physiology underlying diabetic retinopathy.

Aldose Reductase Levels Monitored

Aldose reductase is an important enzyme in the normal metabolism of glucose, which it converts to sorbitol. In people with diabetes, an increase in the concentration of glucose results in greater conversion of glucose to sorbitol, and the increase in cellular concentration of sorbitol is implicated in damage to eyes, nerves, and kidneys.

Dr. Robert Balaban, an NHLBI intramural researcher, has developed a noninvasive method for monitoring the level of activity of aldose reductase in different tissues. He found that a fluorinated derivative of glucose, 3-fluorodeoxyglucose (3-FDG), was converted to fluorosorbitol, and the accumulation of fluorosorbitol could be quantitatively measured by nuclear magnetic resonance spectroscopy. Because 3-FDG is not metabolized by any of the other normal pathways of glucose metabolism, this method can be used to determine the distribution of aldose reductase activity in vivo following the administration of nontoxic 3-FDG. In addition to allowing the determination of tissue levels of aldose reductase in

normal and disease states, the method also can be used to evaluate aldose reductase inhibitor activity in intact tissues. This application may become clinically important, because aldose reductase inhibitors currently are being developed for treatment of diabetes.

Aldose Reductase and Sorbitol Have Important Role in Normal Kidney Function

Dr. Maurice Burg, an NHLBI intramural researcher, has found that the accumulation of sorbitol, through the action of aldose reductase, plays an important role in the mechanisms by which the normal kidney maintains fluid balance. Rats with congenital diabetes insipidus--a disease in which the kidneys produce copious amounts of urine--were studied before and after correction of the disease with vasopressin treatment. Vasopressin is a hormone that normally regulates urine production. Dr. Burg found that treatment with vasopressin increased the levels of aldose reductase activity. The increased activity resulted from an increase in the transcription by the cell of the aldose reductase gene to complementary copies of RNA, which, in turn, led to an increased amount of the enzyme. The sequence of the aldose reductase protein has been determined, and the gene is being cloned in studies to understand gene function and regulation. These studies, although primarily oriented toward the role of aldose reductase and sorbitol formation in normal kidney function, may give important insights into ways to reduce aldose reductase activity in diabetes and thus control the pathologic formation of sorbitol in patients with diabetes.

National Institute of Dental Research

The National Institute of Dental Research (NIDR) supports a variety of research projects on the oral complications of diabetes mellitus and the causes of the disease.

Periodontal Disease Is Associated with NIDDM

Pima Indians have the highest known rate of diabetes in the world. Approximately 50 percent of them past the age of 35 have NIDDM. The main oral complication is severe, rapidly progressive periodontal disease, which occurs with greater prevalence in this population than in nondiabetic populations. During the past 5 years, a longitudinal study of the oral complications of diabetes in Gila River Pima Indians has been conducted by NIDR grantee Dr. Robert J. Genco and colleagues from the State University of New York at Buffalo, in collaboration with epidemiologists at NIDDK and with the Phoenix Area Indian Health Service. Important findings have been reported regarding tooth loss and the relationship of periodontal disease to other diabetic complications and metabolic control.

The study revealed that Pima Indians with NIDDM had lost an average of 12 teeth compared to 8 for nondiabetic individuals and patients with a borderline abnormality in sugar metabolism. Those with NIDDM were also 15 times as likely as nondiabetic individuals to have lost all their teeth. The percentage edentulous (with no teeth) correlated with the duration of diabetes. The major reason for this tooth loss was periodontal disease and its complications. Periodontal disease also correlated with diabetic retinopathy and level of blood sugar. Pima Indians with NIDDM and retinopathy were 4.6 times as likely to have periodontal disease as those without retinopathy. And patients with poorly controlled fasting glucose levels were 2.1 times more likely to have periodontal disease than those with relatively low fasting glucose level.

Researchers Are Exploring Autoantigens

IDDM results from the autoimmune destruction of insulin-producing beta cells in the pancreas. NIDR intramural scientist Dr. Bellur Prabhaka and colleagues are using recombinant DNA technology to identify, isolate, and characterize various cellular autoantigens from the beta cells involved in this autoimmune process. Isolation of these proteins will help in understanding the pathogenesis of IDDM and may lead to a simple diagnostic test for autoantibodies commonly found in IDDM patients.

National Institute of Neurological Disorders and Stroke

The National Institute of Neurological Disorders and Stroke (NINDS) supports research on the neurological aspects of diabetes: peripheral nerve damage, diabetic neuropathy, and stroke. Ten percent of those Americans diagnosed with diabetes--some 600,000 persons--seek treatment for the pain, tingling, and numbness that neuropathy causes. Diabetes is a major risk factor for stroke, and high blood sugar levels during stroke lead to increased morbidity and mortality.

Investigations of Prevalence and Characteristics

The NINDS is sponsoring a long-term study of neuropathy in patients with diabetes at the Mayo Clinic in Rochester, Minnesota, under a team of co-investigators headed by grantee Dr. Peter Dyck. The study is aimed at determining the frequency, severity, and characteristics of neuropathy among diabetic patients. This unique epidemiologic study measures risk factors at regular intervals over time. The study also assesses neuropathic symptoms (such as pain or numbness) and findings (changes in the speed of the nerves' conduction of impulses) using special approaches. Preliminary data suggest that perhaps 40 percent of diabetic patients do not have findings of neuropathy, another 35 percent have mild findings of neuropathy but no clinical symptoms, a further 23 to 24 percent have clinical symptoms, and only 1 to 2 percent have disabling symptoms. This comprehensive study is also assessing risk factors for the development of neuropathy including the type and duration of diabetes, type and control of therapy, hypertension, and kidney failure.

Early Detection of Neuropathy a Goal

Dr. Robert Mackel, an NINDS grantee at Cornell University Medical College in New York City, is using percutaneous microneurography--a procedure that measures electrical response in individual nerve fibers--in his effort to detect diabetic neuropathy at an early stage. Dr. Mackel has studied diabetic patients with mild neuropathic symptoms, patients with no neurological symptoms, and normal controls. Abnormalities were detected in the afferent fibers of peripheral nerves (fibers conveying impulses from the skin to the spinal cord) in both mildly symptomatic and asymptomatic diabetic patients, indicating that neurological damage begins even before there are clinical symptoms. Nerve fibers in the diabetic patients had decreased ability to react to mechanical stimulation of the skin and increased susceptibility to fatigue. Dr. Mackel is currently testing the hypothesis that disturbances in the nerve cell membrane are responsible for these abnormalities.

Why Do Nerve Fibers Degenerate?

Dr. Dyck at the Mayo Clinc has also studied the neuropathic alterations in human diabetic neuropathy, and has found that the pattern of nerve fiber degeneration implies that hypoxia (reduction of oxygen supply to tissue) may be involved in the genesis of diabetic neuropathy. According to one theory, hyperglycemia--high blood sugar--leads to metabolic alterations that affect blood flow in microvessels, so that delivery of oxygen to the tissue is disturbed. Dr. Dyck's study suggests that structural alteration of microvessels appears to be involved in peripheral nerve fiber damage.

In diabetic neuropathy, increased levels of sodium in the nerves draw in water, causing swelling that cuts off the blood supply to the nerves. In his study of the pathogenesis of toxic and diabetic neuropathies, grantee Dr. Henry Powell of the University of California, San Diego is investigating the enzyme system sodium potassium ATPase, which provides energy for pumping sodium out of the nerves. Dr. Powell and his team have shown that increases of dietary sugar cause an increase in the activity of this enzyme. They have induced diabetes in rats by feeding them large concentrations of sugar (galactose); this, Dr. Powell has found, results in a dose-dependent increase in nerve sodium potassium ATPase. However, the increased activity of this enzyme was not enough to pump all of the sodium and water out of the affected nerves.

In recent years, Dr. Powell's laboratory has been studying the topography of the small blood vessels serving the nerves and their vulnerability to nerve swelling. Using a Cray supercomputer, Dr. Powell has been able to show that significant distortion of these vessels can occur even at relatively low fluid pressures within the nerve cell. The computer modeling studies are all based on data from experimental animals.

Developing New Treatments

Dr. Powell and his associates are treating nerve swelling with drugs that inhibit aldose reductase, the enzyme responsible for water and sugar alcohol accumulation in the nerve. These promising drugs have been shown to reduce the level of sodium in the nerve cell by reducing sugar alcohol levels there. Dr. Powell's team is also using electron microscopy to discover the precise location of aldose reductase. During the past year he has been able to determine the subcellular locations of both aldose reductase and the ATPase mentioned earlier.

In collaboration with the National Eye Institute (NEI), Dr. Powell and his colleagues are studying the efficacy of aldose reductase inhibitors in controlling neuropathy in

dogs. With the primary focus on diabetic neuropathy, NEI intramural scientist Dr. Peter Kador is providing Dr. Powell's group with nerve tissue from dogs. Four different aldose reductase inhibitors will be tested on the nerve tissue, providing a unique opportunity to study diabetic neuropathy and strategies for controlling it in a large animal model. Information gained from this study will also be useful in veterinary medicine, since dogs are very susceptible to diabetes.

National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases (NIAID) supports research on disorders of the immune system, including autoimmune diseases such as IDDM. NIAID grantees at the Howard Hughes Medical Institute laboratory at Yale University in New Haven, Connecticut, and at the National Jewish Center for Immunology and Respiratory Medicine in Denver, Colorado, have been examining the role of certain immune molecules in the development of autoimmune disease. Their work suggests that IDDM may arise from defects in processes operating early in immune system development that weed out immune cells that may be harmful to the body.

Germ-fighting cells called T cells are so named because they arise from cells located in the thymus gland during development. Research has suggested that not all T cells made in the thymus actually develop into mature, functioning T cells. Some appear to be wiped out by selective forces in the thymus and never enter the blood stream or become part of the mature immune system. This selection system is believed to keep potentially harmful T cells from being turned loose on the body. Because of their genetic programming, these particular T cells would be unable to distinguish the body's own cells from those of foreign invaders.

Two NIAID-supported groups are studying the role of an immune system molecule, called I-E, in pruning out unwanted T cells from the immune system. Production of I-E molecules is directed by a cluster of genes called the major histocompatibility complex (MHC). In healthy people, MHC molecules located on certain immune cells work together with T cells to recognize foreign organisms and spur an immune response to fight them.

At the National Jewish Center for Immunology and Respiratory Medicine, NIAID grantee Dr. Ed Palmer and his co-workers have characterized T cells in mice based on the genetically determined attributes of cell-surface molecules called T-cell receptors (TCR). The physical makeup of TCR's, which contain two molecular chains called alpha and beta, is partly determined by specific sets of genes called V-alpha or V-beta. These genes encode segments of the two chain molecules.

Dr. Palmer and his co-workers determined, in three strains of mice, the proportion of T cells that contained receptors encoded by V-alpha or V-beta genes. Among the three strains, the researchers found that the proportion of cells carrying TCR's encoded by distinct V-alpha or V-beta genes varied greatly. The strains that contained the fewest number of T cells with a specific V-beta receptor called V-beta-5 appeared to be those that also produced the MHC molecule I-E. When I-E was present, the number of T cells with V-beta-5 receptors was

low. This suggests that the presence of I-E somehow influences the removal of T cells carrying V-beta-5 receptors from the immune cell population.

Grantee Dr. Charles Janeway at Yale University and graduate trainee Eva-Pia Reich and her colleagues at the Howard Hughes Medical Institute laboratory there looked for the presence of V-beta-5 receptors on T cells taken from non-obese diabetic (NOD) mice. NOD mice have been a good experimental model of IDDM because they naturally develop diabetes by the time they are 4 weeks old. However, NOD mice that have been injected with genes for I-E during fetal development do not develop diabetes.

Reich and her co-workers examined the genetic makeup of TCR's on the surface of T cells taken from NOD mice. They found that receptors on diabetes-causing T cells taken from NOD mice contained segments encoded by V-beta-5 genes. Because these cells were able to induce diabetes when transferred into adult mice normally resistant to the disease, the scientists suggest that T cells containing V-beta-5 receptors may be the cells that attack and damage the pancreas.

Work from these two groups supports the idea that, normally, T cells containing receptors that may trigger an autoimmune response are weeded out during fetal development. The scientists have possibly identified those cells as ones containing T-cell receptors encoded by V-beta-5 genes. Both groups suggest that the presence of I-E in fetal mice selectively deletes T cells containing receptors encoded by V-beta-5 genes, thus protecting against autoimmune reactions later in life.

In animals, and perhaps humans, who do not express I-E-like molecules, potentially damaging T cells may escape this selection process and go on to cause diabetes or other autoimmune diseases. This work supports the strategy for developing IDDM drugs aimed at blocking the specific T-cell receptors.

National Institute of General Medical Sciences

The National Institute of General Medical Sciences (NIGMS) supports research and research training in the sciences basic to medicine. The goal of this basic research is to learn more about the underlying cellular mechanisms involved in various disorders, such as diabetes.

Recently, a group of scientists led by Dr. Harvey F. Lodish, an NIGMS grantee, and Dr. Bernard Thorens at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, identified a protein that transports glucose into the insulin-secreting cells (called beta cells) of the pancreas. This transporter may be a crucial component of a system that permits beta cells to "sense" a rise in glucose level in the blood and respond by secreting insulin. Understanding the mechanism by which beta cells detect elevated blood glucose levels is an important goal for scientists studying diabetes.

Dr. Lodish and his colleagues have found that beta cells are the only pancreatic cells that express one particular glucose transport protein, although they previously found this transporter in liver, kidney, and intestinal cells. The special characteristics of this transporter, particularly its precise affinity for glucose, seem to explain the behavior of normal beta cells.

The researchers have also determined that the transport molecules are clustered in a particular part of the beta cells' surface called the microvilli, which are minute, brushy cellular projections. The microvilli are located on the cells' outer membrane, which is an ideal position for glucose uptake. The researchers believe that this discovery may aid studies of the specific interactions membrane proteins in the microvilli have with other parts of the cell, especially its internal "skeleton."

National Institute of Child Health and Human Development

Diabetes in pregnancy can cause problems in an infant whether the diabetes predates the pregnancy or appears during it (gestational diabetes). For this reason, the National Institute of Child Health and Human Development (NICHD) is active in diabetes-related research.

Among the Institute's projects in this area is the long-term Diabetes in Early Pregnancy Study (DIEP), a multi-center project involving more than 1,000 pregnant women. The study, headed by NICHD's Dr. James Mills, continues to yield important data. One promising finding from the DIEP was that diabetic women who entered the study within 21 days after conception and who adhered to strict glucose control for the rest of their pregnancy suffered no more spontaneous abortions than did the control (nondiabetic) women.

Good glycemic control and successful pregnancies were also found to be linked by Dr. Reginald C. Tsang of the University of Cincinnati in Ohio. In his study, Dr. Tsang found that all diabetic patients who had experienced a miscarriage had a successful second pregnancy following appropriate diabetes education and prenatal counseling. Also, in a group of patients who had careful, specific management of their diabetes, the risk for birth trauma associated with macrosomia (abnormally large infant body size, the risk of which is increased with maternal diabetes) was significantly reduced.

Colleagues of the late Dr. Norbert Freinkel of Northwestern University, Chicago, Illinois, are continuing a study of the natural course, history, and development of gestational diabetes. Preliminary results of data accumulated on 241 pregnant women indicate that maternal age at diagnosis, severity of glucose intolerance (the extent of the abnormality in the body's response to glucose), and maternal weight are significant determinants of the status of glucose tolerance after delivery. However, the strongest predictors of glucose tolerance after delivery are the measurements of blood levels of insulin 15-minute and 3-hour after a glucose dose at the time of diagnosis of gestational diabetes.

Investigators headed by Dr. Victor Wynn at the University of London, England, have found a small degree of impaired glucose tolerance in women who were taking oral contraceptives, including those who were being given the new triphasic oral contraceptive which consists of two hormones with a dosage regimen that changes three times a month.

In addition to providing further data on the metabolic effects of oral contraceptives, the English metabolic laboratory has quantified the metabolic effects induced by various brands and doses of oral contraceptives. Results from data previously obtained from 2,800 women are being reassessed

with data from an additional 1,200 women who have been given oral glucose tolerance tests with insulin and lipoprotein assays. Comparisons of nearly 10 brands of oral contraceptives are being made, with particular focus on dose-effects and potency differences.

Studies at the University of Southern Califcrnia and the University of London are attempting to determine whether there are women who have generalized changes in metabolism suggestive of an intolerance to oral contraceptives. Changes with contraceptive use consisting of impaired glucose tolerance with concomitant lipoprotein alterations have been linked in past research to heart disease.

While results so far indicate that some women who use high-dose, high "potency level" progestogen preparations do appear to become insulin resistant during oral contraceptive use, the insulin resistance appears to be compensated for by an increased delivery of insulin from the pancreas.

The investigators believe that despite some obvious differences in carbohydrate metabolism, these changes are not great enough to cause overt disease during current oral contraceptive use.

National Eye Institute

Of the estimated 11 million Americans who have diabetes, about 10 percent have vision-threatening diabetic retinopathy for which some treatment should be considered. Over the past 13 years, controlled clinical trials supported by the National Eye Institute (NEI) have demonstrated that various laser treatments are highly effective in preventing visual loss from diabetic eye disease. Such treatment is now widely available throughout the United States.

Long before a patient notices blurring of vision from diabetic retinopathy, an eye examination can reveal abnormalities in retinal blood vessels, such as hemorrhages, closure of blood vessels, and leakage of fluid. This leakage may cause edema (swelling) of the macula, the part of the retina that provides sharp, central vision. In advanced diabetic retinopathy, new blood vessels proliferate, rupture, and bleed into the interior of the eye. Diabetic retinopathy is the leading cause of new blindness among middle-aged Americans.

To determine whether laser treatment prevents loss of vision from diabetic macular edema and at what point in disease progression treatment is most effective in preventing visual loss, the NEI initiated the Early Treatment Diabetic Retinopathy Study (ETDRS) in 1979. This multi-center clinical trial of 3,711 patients investigated the appropriate time to apply two types of laser treatment--focal and scatter.

In focal treatment, the laser beam seals leaky retinal blood vessels that cause macular edema. In scatter treatment, the laser beam produces many tiny burns scattered throughout the retina but spares the macula. This reduces the stimulus for abnormal new blood vessels to proliferate and scar tissue to form.

ETDRS researchers also investigated whether 650 milligrams of aspirin taken daily would slow or prevent the development of diabetic retinopathy. According to anecdotal information, the incidence of severe retinopathy seemed lower than expected in diabetic patients taking aspirin for arthritis. Because aspirin slows blood platelet aggregation, the researchers hypothesized that it could affect the patient's blood chemistry and, consequently, the development of retinopathy.

Final ETDRS results, reported in late 1989, support earlier findings by the study that focal treatment of macular edema reduces by one-half the patient's risk of visual loss. The study also showed that, if a patient regularly has eye examinations, scatter treatment may be deferred until high-risk retinopathy develops.

Results of aspirin treatment for diabetic retinopathy demonstrated that the dosage used in the study did not slow or prevent the progression of retinopathy, but neither did it increase the risk of hemorrhage into the vitreous, the clear fluid that fills the eye. The finding that aspirin does not increase risk for hemorrhage is important because diabetic patients have twice the normal risk for developing cardiovascular disease, especially myocardial infarction, which might require daily aspirin therapy.

National Institute on Aging

Noninsulin-dependent diabetes is more common in older people than in any other age group. Thus, the National Institute on Aging (NIA) supports research on this illness as it pertains to aging processes. Two recent NIA findings are based on studies of rodents fed low-calorie diets that retard aging and diseases.

Evidence Supports the Glycation Hypothesis of Aging

NIA grantee Dr. Edward J. Masoro and colleagues at the University of Texas Health Science Center in San Antonio have been testing the glycation hypothesis of aging, which states that glucose may be a mediator of aging processes through its alteration of protein and DNA structure and functions.

Glycation is believed to be significant in the development of complications relating to diabetes because glucose can alter proteins and nucleic acids, leading to cross-linking in connective tissues, blood vessels, eye lens, blood cells, peripheral nerves, and other tissues. Cross-linking is a process that increases in both animals and humans as a function of age. Thus, scientists believe cross-linking--and increased glucose levels--may be responsible for some physical changes that occur in older people who have diabetes.

Dr. Masoro's group found that blood glucose levels in rats fed low-calorie diets were significantly lower than in rats whose diet was unrestricted. Also, they found less linking of glucose to the hemoglobin molecule in the rats on the low-calorie diet. Thus, the reduced glucose levels observed in rats fed low-calorie diets and the fact that these rats have an extended lifespan with a slowing of their aging processes, supports the glycation hypothesis of aging. Glycation reactions are also believed to have a significant role in the development of diabetic complications.

The Effect of a Low-Calorie Diet on the Pancreas

Another NIA grantee studying caloric restriction in rodents is Dr. Roy L. Walford at the University of California, Los Angeles. He recently showed that restriction of calories in mice resulted in lower glucose levels and an altered structure of the pancreas.

Two groups of mice were studied following weaning at 4 weeks. One group was fed a normal diet while the other group was fed a diet restricted in calories. Both groups received equal amounts of minerals, proteins, fats, and vitamins--a diet that was sufficient to satisfy nutritional requirements. Only carbohydrates fed to the two groups were adjusted to provide the difference in calories.

Eleven months later the investigators examined the pancreases of the mice. In those fed the low-calorie diet the volume of the islets of Langerhans (cells that secrete insulin and are found in the pancreas) was significantly smaller. These results indicate that consuming a low-calorie diet reduces the organism's need for insulin, which eases the burden on the process of metabolizing foods.

Division of Research Resources

The Division of Research Resources (DRR) supports a wide range of research aimed at better controlling the complications of diabetes. One of these is diabetic glomerulopathy, a degenerative disease of the kidneys that often forces patients to seek kidney transplants. Unfortunately, the same degenerative process can attack transplanted organs.

According to DRR grantee Dr. Michael W. Steffes at the University of Minnesota General Clinical Research Center (GCRC) in Minneapolis, the degenerative disease can be controlled by the transplant of pancreatic tissue. This tissue generates the insulin needed to control glucose levels, which, the grantees theorize, is the key to halting lesion development.

Using the Minnesota GCRC, Dr. Steffes and his colleagues obtained and analyzed biopsies--small samples of tissue--from kidneys soon after they were transplanted into 12 patients with insulin-dependent diabetes mellitus (IDDM). Each of the patients received pancreatic tissue transplants 1 to 7 years later. Kidney biopsies were again performed about 4 years after the pancreatic tissues were transplanted.

The researchers found that lesions seen on the first biopsies had stopped progressing after the pancreatic transplant. Biopsies that showed no evidence of glomerulopathy soon after kidney transplantation showed only moderate signs of the disease on the second biopsies. Patients receiving pancreatic tissue also had smaller lesions than a set of matched diabetic patients who received kidney but not pancreatic transplants.

The investigators believe that normal blood glucose levels, brought about by the transplant of healthy pancreatic tissue, can prevent the progression of diabetic glomerulopathy in transplanted kidneys.

National Center for Nursing Research

Diabetes research supported by the National Center for Nursing Research (NCNR) focuses on finding new ways to help patients maintain optimum control over symptoms by promoting adherence to treatment regimens and by helping people adjust to the physical, psychological and social effects of the disease.

Patients with NIDDM Need to Verify Symptoms with Blood Test

Patients' detection and regulation of their blood sugar levels are crucial to management of NIDDM. However, many people with this disease make decisions about self-regulation based on symptoms they believe to be related to high or low blood sugar levels without using a blood test for verification.

Dr. Edna K. Hamera and her colleagues at the School of Nursing, University of Kansas, Kansas City, studied 51 patients who believed that certain frequently occurring symptoms were related to their blood sugar levels. The NCNR grantee and her colleagues found that 12 percent of the patients could fairly accurately interpret their symptoms for low blood sugar. Most, however, identified symptoms that were either not related to blood sugar or were related but incorrectly interpreted by the patient. Those patients who were more accurately able to recognize symptoms of low blood sugar had better disease control during the study period.

Since patients with NIDDM are taught to eat when blood sugar is low, misinterpretation of symptoms regarding low blood sugar influences some patients to eat when their blood sugar is not low. Often this means deviating from the prescribed weight reduction, low-calorie diet and contributing to a decrease in metabolic control.

This study verifies earlier research and indicates that health care providers should continue to discourage the use of symptoms as the only indicators of blood sugar levels, and should instruct patients to test their blood before taking action.

Researchers Study Effects of Personality and Coping Methods on Adaptation to IDDM

NCNR grantee Dr. Susan E. Pollock, of the School of Nursing, University of Texas at Austin, is studying how methods of coping with stress, as well as attitudes toward change and challenge, affect successful adaptation to IDDM. Dr. Pollock and her colleagues are measuring the influence of

personality traits, such as having a sense of control over life events, having a strong sense of self-worth, and welcoming changes and challenges on managing the physiological, psychological and social effects of IDDM.

The investigators will assess the patients' levels of functioning at work and in their home lives, their use of social support systems, and their methods of handling psychological stress. Learning more about the personality traits that may predict successful adjustment to IDDM can enable nurses and other health care workers to find ways to minimize many of the problems that may result from the disease.

Use of Contracts to Increase Patient Compliance to Treatment Regimens is Studied

One method nurses can use to increase patient compliance to treatment regimens is to develop a contract between patient and nurse. NCNR grantee Dr. Susan Boehm, at the School of Nursing, University of Michigan, Ann Arbor, is assessing the success rates of three approaches to patient contracting and comparing them with success rates for patients who do not sign contracts. The study will include 300 men and women with NIDDM who are being treated in a diabetes care center.

One group of patients will contract for compliance behaviors such as taking medications, maintaining diet restrictions, and losing weight and exercising. Another group will contract for these types of behaviors using specific strategies to achieve them, such as asking a family member to remind the patient to take medications. A third group will receive training in behavioral techniques for maintaining treatment regimens and will contract for specific strategies to achieve them. To further encourage patient compliance, each contracting patient will choose a "reinforcer" to receive if the contract is kept. A control group will not sign a contract. This study has the potential to provide nurses with more effective methods to improve patient compliance.

Outlook

Information about how diabetes occurs and how it causes complications will ultimately be the basis for developing a new means of preventing and curing all forms of diabetes. The advances now being achieved are due in large part to the successes of research in fields such as genetics, cell biology, and immunology. While recent progress in diabetes research has been exciting, this disease remains a major public health problem. The only hope for sparing the millions who will otherwise suffer from diabetes in the future is continued research. The future of research depends in large part on recruiting and training young scientists, especially young physicians trained in research methods. Attracting the young to research careers, in turn, depends on the availability of a pool of students educated in scientific fundamentals and a public knowledgeable enough about science to understand its role in the future of the nation's health.

CENTERS FOR DISEASE CONTROL

Diabetes Translation

Approximately 6 million Americans have been diagnosed with diabetes. Diabetes is a chronic, complex, metabolic disease characterized by high blood glucose levels caused by a deficiency in insulin production, an impairment of insulin utilization, or both. Survey data indicate an additional 5 million persons may unknowingly have the disease. Each year more than 500,000 new cases of diabetes are identified.

Diabetes is the sixth leading underlying cause of death due to disease, causing the death of 36,000 Americans and contributing to over 100,000 additional deaths. This also is probably a substantial underestimation, because diabetes is reported on only about half the death certificates of persons who die with the disease and is listed as the underlying cause on only one quarter of the certificates where it appears.

Individuals afflicted with diabetes face not only a shortened life span, but also the probability of incurring acute and chronic complications. Persons with diabetes spent approximately 11 million days in the hospital. A conservative estimate of the cost attributable to diabetes is $20.4 billion. Even so, the full economic impact is masked because additional medical expenses are often attributed to the specific complications of diabetes rather than to the disease itself.

Approximately 50,000, or half of all nontraumatic amputations in the United States occur in people with diabetes. It is the leading cause of new cases of adult blindness.

The disease is not only an independent risk factor for cardiovascular disease, but it also interacts with other risk factors--smoking, high blood pressure, cholesterol, obesity, and physical inactivity--so that heart disease is twice as common and more often fatal in people with diabetes than in the general population. The risk of atherosclerotic disease is five times greater in women with diabetes. Approximately 50 percent of the people with diabetes have hypertension, compared to 20 percent of those without diabetes.

Diabetes accounts for 9,000, or 30 percent, of the total new cases of end-stage renal disease in the United States each year. Women with diabetes have increased complications of pregnancy and their babies are more likely to die at birth. Infants of diabetic mothers also have a threefold increase in the frequency of birth defects, and a fivefold increase in other complications that require intensive medical care in the early days of life.

In an effort to reduce the health and economic burdens of diabetes, the Centers for Disease Control (CDC), in partnership with 29 States and one territory, is conducting a wide range of activities to:

- Implement effective control strategies at the community level
- Establish consensus concerning standards for patient management and self-care
- Develop networks for rapid translation of advances in care into community practice
- Create the operational base upon which intervention strategies can be built
- Evaluate program impact on reducing selected complications

These State programs have been working closely with various public, private, and voluntary organizations, as well as with service delivery programs, to prevent complications associated with diabetes including blindness and visual loss, adverse outcomes of pregnancy, and lower extremity amputations (LEAs). The programs also target hypertension, which is more than twice as prevalent among people with diabetes as it is in nondiabetic populations. Hypertension is strongly associated with cardiovascular and cerebrovascular disease, the chief causes of premature death in diabetes.

The efforts supported by CDC at the State level emphasize the delivery of state-of-the-art services to minority, elderly, and other low socioeconomic groups disproportionately affected by diabetes. To target essential services to those in need, 65 percent of the State programs, with CDC assistance and leadership, have secured third party reimbursement for outpatient health education for people with diabetes.

CDC chairs the Financing Coordinating Committee that works with the Health Care Financing Administration and the Health Insurance Association of America to improve essential health care services for persons with diabetes. Committee members include representatives from the American Diabetes Association, American Association of Diabetes Educators, American Dietetic Association, and National Diabetes Advisory Board.

In 1988 Congress appropriated nearly $2.4 million in additional funds to the diabetes effort at CDC to initiate a more intensive effort to rapidly and effectively "translate" research findings into patient care. On the recommendation of the National Diabetes Advisory Board, the program developed and implemented a host of applied science projects. These include:

- Studies to evaluate screening for increased urinary albumin as a risk marker for diabetic renal disease and the short-term efficacy of preventive interventions. Findings will be used to target efforts to prevent or delay end-stage renal disease in diabetes.
- Studies to develop and evaluate comprehensive primary care and public health strategies to decrease risk factors for lower extremity amputation and to improve the prevention behaviors of providers and patients. Findings will enhance programmatic efforts to prevent amputation.

- A study to ascertain the current vision of diabetic patients entered 2 or 3 years ago into programs to prevent visual loss and to determine how well they complied with treatment and examination recommendations findings will assist CDC to gauge its impact, adjust efforts accordingly, and determine if its efforts are resulting in a lasting change (at least for an intermediate period).

- Studies to evaluate utilization and cost-effectiveness of prepregnancy counseling among women with diabetes to decrease maternal and infant morbidity and mortality.

Revision, expansion, and updating of the 1984 publication, The Prevention and Treatment of Five Complications of Diabetes: A Guide for Primary Care Practitioners is scheduled for completion in the spring of 1990. The Guide represents practical management guidelines for the prevention and treatment of nine major complications of diabetes.

In addition, CDC is introducing an annual diabetes surveillance report on the incidence and prevalence of diabetes and its complications that will not only help in planning activities, but also allow health agencies to better measure, at less expense, their impact on the disease and its sequelae. CDC is cooperating with three State health agencies to develop similar surveillance systems at the State level.

Diabetes Today is a course recommended in the National Long-Range Plan to Combat Diabetes, 1987. The purpose of the course is to improve dissemination of the existing and emerging knowledge base about all components of an effective community strategy. The CDC is currently developing the course, with a target date for pilot testing in the fall of 1990.

CENTERS FOR DISEASE CONTROL

National Center for Health Statistics

DIABETES

Information from the National Vital Statistics System indicates that diabetes mellitus was the seventh leading cause of death in the United States in 1987, accounting for over 38,532 deaths or 1.8 percent of all deaths in the year. Since 1978 the risk of death for this cause has levelled off from an earlier downward trend. The risk of death from diabetes is about the same for males as for females, but over twice as high for the black as for the white population.

The basis for determining the total prevalence of diabetes mellitus in the United States adult population 20-74 years of age was obtained for the first time in the second program of the National Health and Nutrition Examination Survey as an aid to the increased authority of the National Institutes of Health and Centers for Disease Control (Public Law 93-354) for diabetes prevention, control, research and training. The diagnoses for the prevalence estimates were obtained from the physical examination; medical and dietary history; and blood and urine tests conducted as part of the diagnostic glucose tolerance test given to a probability sample of those adult examinees not presently taking insulin. Findings indicate that the total prevalence of diabetes is approximately 6.6%, or two times that for known diabetes. Similar data were collected in the Hispanic Health and Nutrition Examination Survey, and are being collected for the third National Health and Nutrition Examination Survey, which began in October of 1988. NHANES III includes additional laboratory measurements related to diabetes.

Findings from the Hispanic Health and Nutrition Examination Survey indicate a total prevalence of diabetes of 24 percent among Mexican Americans ages 45-74 in the Southwest, of 16 per cent among Cubans ages 45-74 years in the Miami area, and of 26 per cent Puerto Ricans ages 45-74 years in the New York metropolitan area.

In 1976, the National Health Interview Survey (NHIS) collected prevalence data on diabetes by numerous demographic population characteristics. In addition to determining the prevalence of known diabetes in the population, the 1976 NHIS asked for the type of medication and level of knowledge about this condition among individuals reported to have diabetes. Diabetes prevalence data are collected on a continuous basis by the NHIS. Based on data now available from the NHIS, in 1988 nearly 6.2 million persons in the civilian, noninstitutionalized population were reported to have known diabetes, reflecting a rate of 25.8 conditions of known diabetes per 1,000 population. Extensive data from the 1979-81 NHIS and other diabetes - related data were included in Diabetes in America, a publication sponsored by the National Diabetes Data Group of the National Institute of Arthritis, Diabetes, Digestive

and Kidney Diseases of NIH.

According to the 1988 National Hospital Discharge Survey, an estimated 454,000 patients were discharged from short-stay hospitals in the United States with a first-listed diagnosis of diabetes mellitus. The average length of stay for these patients was 8.2 days. Females accounted for 54 percent of the discharges and patients 45 years and over accounted for 66 percent of the discharges.

Alcohol, Drug Abuse and Mental Health Administration

NIMH Diabetes Activities

The National Institute of Mental Health (NIMH) supports studies on psychosocial, behavioral and biological risk factors and their interactions in diabetes. The Institute also supports research on the psychiatric complications of the illness and on psychosocial and behavioral treatment and interventions for diabetes.

NIMH researchers are investigating whether adults with Insulin-Dependent Diabetes Mellitus (IDDM) experience higher rates of cognitive impairment than non-diabetic matched controls. The study is delineating potential risk factors for impairment including sociodemographic, medical and psychiatric factors. Additionally, subgroups at increased risk for cognitive impairment will be identified and specific interventions developed for these populations.

Other NIMH investigators are examining adaptive family processes in diabetes. This knowledge is a vital prerequisite to construction of effective, empirically based primary and secondary intervention programs to enhance and maintain family adaptation, especially in the context of parental dysfunction. In a longitudinal study, NIMH researchers are investigating the complex interplay between ego development and family environments in juvenile diabetics. This study has significant implications for clinical interventions through clarifying the impact of chronic illness upon adolescents and their families as well as to elucidate developmental influences upon illness management.

Additionally, NIMH researchers have focused on understanding how stress and behavior influence the onset and course of diabetes mellitus. Research in this area involves both animal and human studies. In the animal research programs, the investigators have attempted to discover whether stress effects the onset and course of non-insulin-dependent diabetes mellitus by examining the effects of mild environmental stress on normal animals and on animals with a genetic predisposition to develop non-insulin-dependent diabetes mellitus (NIDDM). This research has demonstrated in at least one animal model of this disease that stress appears to be a necessary ingredient for the appearance of hyperglycemia. Further, the researchers have been able to identify an abnormality in the autonomic nervous system of these animals which may be responsible for this stress sensitivity. In both animal and human studies the investigators have demonstrated that behavioral and pharmacologic stress-reducing therapies seem to improve hyperglycemia in this form of diabetes. Their work has been supported by recent research on animals and humans done

in other laboratories which also suggests that an autonomic nervous system defect is part of the pathophysiology of NIDDM. This work is extremely important in that it suggests a whole new array of pharmacologic and behavioral alternatives to the treatment of NIDDM.

In another line of research, investigators have begun to identify individual psychological differences which predict the degree to which conventional insulin therapy will establish good glycemic control in children with IDDM. Researchers have established that a Type A behavior pattern is predictive of a hyperglycemic response to a competitive stress. Most recently, they have identified another psychological factor (introversion) as a variable which correlates with the degree of blood sugar control over an extended period of time.

NIMH intramural scientists are involved in basic studies of the biochemistry of insulin and the expression of genes for insulin in the brain and peripheral tissues.

The NIMH has a strong commitment to research on health and behavior particularly on the examination of biological, psychosocial and behavioral factors and their interactions that impact on the development and course of medical illnesses. Additionally, psychosocial, psychopharmacologic and behavioral treatments and interventions are another focus for behavioral medicine research programs.

INDIAN HEALTH SERVICE

Diabetes Program

The National Commission on Diabetes recommended, and Congress authorized and funded in 1979, the IHS Model Diabetes Health Care Program. The program has developed and evaluated effective and culturally acceptable methods to reduce the severity of the disease. The program has also started methods to reduce the expense to the IHS of related medical services.

Five initial project sites were chosen to represent different types of IHS facilities and different population groups. The Claremore (Oklahoma) Indian Hospital is a multi-service referral facility located off the reservation. The Fort Totten (North Dakota) Health Center is a reservation-based clinic. hospital with outlying clinics on the Pima reservation. The Sacaton (Arizona) program uses a small (Nebraska) hospital with outlying clnics on the Pima reservation. The Albuquerque (New Mexico) program serves both urban and rural Indians.

Two additional projects were initiated in FY 85. The Maine Intertribal Diabetes Prevention and Care Project is a coordinated effort among four tribes under contract to IHS. The Lummi Service Unit is the base for a multidisciplinary team providing service to northwest Washington. During FY 87, two new Centers of Excellence were developed: one in Browning, Montana and one in Tuba City, Arizona. These sites are developing culturally relevant approaches to diabetes education among the Plains Indians and the Navajo. Two "model" sites have received recognition of the Diabetes Education Programs through the American Diabetes Program Association.

Additional budget mark-ups in FY 88 provided the funds for these new programs in northern Minnesota, Alaska, and Arizona which are now operating. Multidisciplinary teams have been placed at each site to upgrade preventive services and to develop a comprehensive diabetes care plan that includes routine screening for complications, patient education, nutrition counseling, and attention to related conditions such as hypertension, urinary tract infections, and foot care. Considerable progress has been made at these sites in delivering high-quality, culturally acceptable diabetes care.

Transfer of effective treatment strategies from model projects to service units wss an ongoing priority in 1989. Diabetes Control Officers in all areas provided surveillance, training, and program reviews to ensure timely application of techniques piloted in the model sites. Materials developed by the "model" sites have been very popular system wide. In 1989 audit data from 94 facilities was collected to monitor quality assurance in diabetes care.

Progress is also being made in community involvement. A training module for Community Health Representatives is available. A foot care manual is now being printed for instructing Community Health Representatives in basic foot care. A physician orientation package developed in 1989 is available.

The future plans for the Diabetes Program include the development and evaluation of on-going surveillance system for complications of diabetes including End Stage Renal Disease and amputations. IHS will implement a Type II Diabetes teaching curriculum and develop the Indian-oriented material related to the curriculum. Criteria for the National Diabetes Education Standards were modified for IHS in 1989 and will be used to guide and evaluate education efforts. In addition, a resource manual will be distributed to guide practitioners counseling patients who are using the commodity foods programs.

In FY 90, five new sites will be added in Ft. Berthold, Zuni, California, Utah, and Oregon. Technical aspects of several programs including the Headquarters capability will be strengthened. A major cooperative initiative with NIH was initiated with a conference involving diabetes researchers, Indian tribes, and IHS.

DIGESTIVE DISEASES
Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
National Institutes of Health:					
National Institute of Diabetes and Digestive and Kidney Diseases	$95,597,283	$102,259,000	$103,236,000	$106,750,000	$111,100,000
National Cancer Institute	68,631,000	75,805,000	87,011,000	90,164,000	94,211,000
National Heart, Lung and Blood Institute	7,294,000	7,232,000	6,288,000	6,450,000	6,700,000
National Institute of Dental Research	2,308,000	16,557,000	17,136,000	17,753,000	18,410,000
National Institute of Neurological Disorders and Stroke	988,000	1,364,000	2,085,000	2,152,000	2,251,000
National Institute of Allergy and Infectious Diseases	33,883,000	35,185,000	38,435,000	39,348,000	41,499,000
National Institute of General Medical Sciences	2,385,000	4,428,000	4,545,000	4,600,000	4,600,000
National Institute of Child Health and Human Development	5,518,000	6,163,000	6,205,000	6,500,000	6,800,000
National Institute of Environmental Health Sciences	7,813,000	8,793,000	9,836,000	10,190,000	10,587,000
National Institute on Aging	1,685,000	1,492,000	1,926,000	1,993,000	2,072,000
Division of Research Resources 1/	17,705,000	14,393,000	13,898,000	12,165,000	11,988,000
National Center for Nursing Research	320,000	65,000	321,000	360,000	360,000
Office of the Director 2/	544,000	1,224,000	525,000	583,000	147,000
Total, NIH	244,671,283	274,960,000	291,447,000	299,008,000	310,725,000

1/ This includes RCMI awards. Prior to FY 89, RCMI's were shown in OD.

2/ This includes AREA awards for FY 1987 - 1991, and RCMI awards for FY 1987 and 1988.

NATIONAL INSTITUTES OF HEALTH

National Institute of Diabetes and
Digestive and Kidney Diseases

DIGESTIVE DISEASES

Digestive diseases such as peptic ulcers, gallstones, and liver disorders constitute a major health problem in the United States today. Twenty million Americans are treated for some type of chronic digestive disease each year, and according to the National Digestive Diseases Advisory Board, almost half of the U.S. population will suffer a digestive problem at some time.

For more than 35 years, the efforts of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) have contributed to better diagnosis, treatment, and prevention of digestive diseases.

The development in the 1970's of new drugs such as cimetidine, ranitidine, and sucralfate has improved dramatically the outlook for people with peptic ulcers. In fact, the number of hospitalizations for this condition dropped 43 percent between 1970 and 1980.

Until the early 1980's, the 1-year survival rate for liver transplant patients was about 30 percent. However, with improvements in surgical techniques and the introduction of the powerful anti-rejection drug cyclosporin, survival after organ transplantation has markedly improved. Today, the 1-year survival rate for liver transplant patients ranges from 70 to 90 percent.

In addition to NIDDK, other institutes at the National Institutes of Health (NIH) conduct and support research into digestive diseases. These include the National Cancer Institute; the National Heart, Lung, and Blood Institute; the National Institute of Dental Research; the National Institute of Neurological Disorders and Stroke; the National Institute of Allergy and Infectious Diseases; the National Institute of General Medical Sciences; the National Institute of Child Health and Human Development; the National Institute of Environmental Health Sciences; the National Institute on Aging; the National Institute of Deafness and Other Communication Disorders; the National Center for Nursing Research; the Division of Research Resources; and the NIH Office of the Director.

Liver Diseases

The liver performs many complex biochemical tasks. As the largest internal organ in the human body, the liver functions as a chemical factory, producing proteins, such as the major clotting factors that prevent a person from bleeding to death, that circulate in the blood. The liver also purifies and detoxifies blood and secretes fluids, such as bile, that aid in digestion and waste removal. The liver is particularly vulnerable to many types of disease, and each year over 25,000 Americans die from chronic liver disorders.

UW Solution Improves Organ Preservation and Graft Survival in Liver Transplantation

Even though transplantation of the human liver has become much more effective in recent years, a critical shortage of donor organs still exists. Consequently, there is a vital need to develop more reliable methods of extending the preservation time of donor livers before transplantation. Until recently, the maximum period of liver preservation was 8 hours or less through cold storage in the standard Euro-Collins solution.

NIDDK grantees Drs. Folkert O. Belzer and James Southard at the University of Wisconsin Medical Center in Madison have developed a new preservative called the UW solution, which can keep a donor liver viable for up to 30 hours. In a study that analyzed the results of 185 human liver transplants preserved with UW solution compared with 180 grafts using the Euro-Collins solution, the researchers found that the average preservation time of the UW-preserved livers (10.1 hours) was almost twice as long as that of the Euro-Collins preserved livers (5.9 hours). UW-preserved grafts also survived at a higher rate (76 percent graft survival at 3 months using UW-preserved livers versus 68 percent using Euro-Collins-preserved livers).

Extended preservation time provides important benefits for the safety of patients, for the timing of surgery, for better coordination of surgical teams, and for prospective cross-matching between donor and recipient. In addition, more time allows for organ retrieval from more distant locations, and it permits more preparation time for staff in anesthesia, nursing, operating room, blood bank, and intensive care units. Development of the UW solution is a substantial advance over traditional preservatives.

New Screening, Diagnostic, and Monitoring Method for Primary Biliary Cirrhosis

Primary biliary cirrhosis (PBC) is a rare liver disease of unknown cause that most often affects women. PBC is characterized by chronic inflammation and gradual destruction

of the small bile ducts, which ultimately lead to liver failure. The majority of patients with PBC have antibodies to their own mitochondria (a structure that provides energy for metabolism and is found in all cells of the body). These antibodies can be detected through blood tests in order to screen, diagnose, and monitor these patients. Current methods for the detection of these antibodies lack specificity (resulting in false positives) and sensitivity (resulting in false negatives), and they are time-consuming and not readily available.

NIDDK grantees Dr. M. Eric Gershwin at the University of California, Davis and Dr. Rolland Dickson at the Mayo Foundation, Rochester, Minnesota and associates have developed an enzyme-linked immunoassay to quantify specific mitochondrial antibodies. Instead of using mitochondria extracted from cells for the test, they produced the specific mitochondrial protein to which the antibodies are directed. They made this protein by the new techniques of molecular biology, gene splicing and recombinant DNA cloning. The assay using this mitochondrial protein is more practical and sensitive than previous methods.

The investigators analyzed 217 serum samples from 93 patients with PBC and 124 patients in a control group for reactivity in the immunoassay. The results showed that 89 of 93 patients with PBC reacted in the test, whereas no subjects in the control group showed a significant reaction. This indicates that the use of recombinant, DNA-produced proteins provides a simple, accurate, and rapid method of quantifying and monitoring the levels of specific mitochondrial autoantibodies in the serum of patients with PBC. This research advances the study of autoimmunity significantly and promises to open new avenues of investigation into the causes of PBC.

Safe, Effective Treatment for Brain Dysfunction and Coma Due To Liver Failure

When the human liver fails, a person may develop impaired brain function and lapse into a coma, and possibly brain death, a common cause of death in liver failure. Scientists have long speculated about the possible causes of coma in patients with liver failure. One reason they have suggested is that, as the liver fails, it ceases to make some substance needed by the brain. According to another hypothesis, the ailing liver may fail to remove some necessary neuroactive substance from the blood.

NIDDK intramural scientist Dr. E. Anthony Jones and his associates have been able to reverse liver coma in animals by administering flumazenil, a drug normally used to reverse the action of benzodiazepines (tranquilizers such as Valium). The scientists have found that patients in liver coma have an

abnormality in the brain receptors for benzodiazepines. In studies conducted in rabbits and rats with liver failure, the researchers have found behavioral and physiological changes that confirm the existence of a substance that binds to the benzodiazepine receptors in the brain. The investigators suggest that this tranquilizer-like substance, which the failed liver cannot eliminate, causes brain dysfunction. The scientists are continuing studies to identify and isolate the substance.

Human trials of flumazenil are planned, and if the treatment is found successful, it will most likely benefit those patients with chronic low-grade liver failure by sparing them the prolonged periods of incapacity caused by poor brain function and coma. These patients will also benefit nutritionally, because they will no longer be required to restrict their intake of protein, too much of which can induce coma.

Interferon Therapy Proves Effective for Non-A, Non-B Hepatitis

Non-A, non-B hepatitis (NANBH) is the most common form of hepatitis caused by blood transfusions. The disease is also common among persons who are exposed to blood or serum, such as illicit drug abusers or medical care workers. Although many cases of NANBH are mild, about 15 to 25 percent result in serious liver injury, which can lead to cirrhosis and liver failure.

NIDDK intramural scientist Dr. Jay Hoofnagle and his colleagues have completed a randomized, double-blind, controlled clinical trial of a genetically engineered form of interferon in patients with hepatitis. Interferon is a naturally occurring, disease-fighting substance produced by the immune system. The NIH scientists treated 41 patients, half with alpha interferon and half with a placebo, administered 3 times weekly for 6 months. Approximately 75 percent of the patients who received interferon showed a significant improvement in liver function.

While many patients benefited from this therapy, they tended to relapse when interferon was discontinued. Current studies are analyzing the effects of treatment for longer periods with higher doses of interferon. Future studies will focus on improving the long-term response rate, perhaps by using a combination of other antiviral agents administered with interferon.

Diagnostic-Therapeutic Techniques

Medical care for intestinal disorders has advanced greatly over the last decade through developments in fiberoptic instrumentation that led to the flexible endoscope. The endoscope has changed from a solely diagnostic device to a therapeutic tool that enables physicians to inspect and treat numerous bowel and other digestive disorders. The decade has also seen many other advances in screening, diagnosis, treatment, and prevention of intestinal diseases. Ultrasound, for example, has been applied endoscopically to add a new dimension to the diagnosis of gastrointestinal disease.

Echo Probe Provides a Powerful New Diagnostic Tool

The endoscopic echo probe is an improved technique in which high frequency, high resolution ultrasound images are obtained from the intestinal tract using an ultrasound probe in the tip of a fiberoptic endoscope. This instrument, developed by NIDDK grantee Dr. Fred Silverstein and his associates at the University of Washington in Seattle, is more sophisticated than previous devices and provides a powerful new tool for diagnosis, management, and investigation of patients with gastrointestinal diseases.

Dr. Silverstein and his colleagues have conducted 3 investigations in which they used the echo probe successfully to detect colon cancer in 88 percent of cases. The probe enabled the researchers to determine the depth of invasion of cancer cells in 93 percent of these cases. The instrument can be used to diagnose and to determine the stage of diseases by observing changes in the thickness of the intestinal wall, changes in normal layers of the wall, and the appearance of lesions. The endoscopist can also estimate the size and depth of ulcers. Information obtained with the instrument can help the physician determine optimal therapies for cancer and other diseases.

The investigators are also attempting to adapt the echo probe to provide real-time images that more effectively show motility (movement of contents) within the digestive tract. This capability could provide new means of assessing disorders of motility and of studying the pathophysiology of diseases such as achalasia (regurgitation because of failure of nerves that control swallowing), diabetic gastroparesis (a diabetic complication affecting stomach function), and irritable bowel syndrome.

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Effective Therapeutic Endoscopic Techniques Determined by Consensus Panel

Various approaches for using therapeutic endoscopy to manage bleeding ulcers have evolved in recent years with particular emphasis on managing high-risk patients. Bleeding is a serious complication of peptic ulcers and is a common cause of emergency hospitalization in the United States. To define the appropriate role of the various methods, NIDDK and the NIH Office of Medical Applications of Research recently held a Consensus Development Conference on Therapeutic Endoscopy and Bleeding Ulcers. The consensus panel, drawn from experts in the field, determined that the two most effective techniques are multipolar electrocoagulation, the use of electrical current to cauterize bleeding tissues and the heater probe. Both of these methods were found to stop bleeding promptly and to prevent re-bleeding in actively bleeding patients. The panel also determined that laser photocoagulation and injection therapies appear to be effective but require further evaluation.

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Gallstones

Approximately 20 million Americans have gallstones, and some 500,000 gallstone operations are performed annually in the United States at an estimated cost of $5 billion. Surgical removal of gallstones is the safest and most effective means of treatment in most cases, but nonsurgical methods are becoming increasingly important, particularly in patients for whom surgery is risky.

Nonsurgical Treatment of Gallstones Found Effective

Institute grantees Dr. Leslie Schoenfeld of Cedars-Sinai Medical Center in Los Angeles, California and Dr. Alan Hofmann of the University of California in San Diego were pioneers in researching, over the past 16 years, the effectiveness of bile acids, namely chenodeoxycholic acid (CDCA) and ursodeoxycholic acid (UDCA), in dissolving gallstones. Dr. Jay W. Marks and his associates at Cedars-Sinai Medical Center and at the University of California in Los Angeles have also demonstrated the ability of UDCA to prevent gallstones in obese patients during rapid weight loss.

NIDDK grantee Dr. Johnson Thistle and his colleagues at the Mayo Foundation in Rochester, Minnesota have successfully dissolved cholesterol gallstones in patients using methyl tert-butyl ether (MTBE), a common laboratory solvent. The technique involves placing a thin, flexible tube into the gallbladder and flushing it with small amounts of MTBE. More than 95 percent of stones were dissolved in 72 of the 75 patients treated with MTBE. Among 21 patients whose stones were completely dissolved, only 4 experienced recurrences of stone formation within 16 months. Among 69 consecutive patients treated successfully with the method, only 1 required subsequent surgery for gallstones. The investigators concluded that MTBE therapy for stone dissolution is a safe and effective treatment in selected patients with gallbladder stones.

Obesity

Body Composition Linked to Risk of Heart Disease in Obesity

NIDDK grantee Dr. F.X. Pi-Sunyer and his colleagues at St. Luke's Roosevelt Institute for Health Sciences in New York City are studying differences in body composition and energy metabolism in lean and obese subjects.

The researchers measured energy expenditure in two groups of men who were matched with respect to total body weight (130 to 165 percent desirable body weight). One group was obese (30 percent body fat) while the other group was lean (10 percent body fat) but highly muscular. The lean subjects had significantly greater capacity for energy expenditure during

resting metabolic rate tests as well as increased energy expenditure following a meal.

The investigators conducted another study to find out whether the differences in energy expenditure between the groups were due to leanness in one group or fatness in the other group. This time the scientists chose groups that had the same amounts of lean tissue, but who differed in their body fat contents (13 percent and 30 percent body fat). Although resting metabolic rate was not found to be different for these groups, energy expenditure was low in the obese group, indicating that body fatness, rather than the amount of lean tissue, is the major determinant of energy expenditure following a meal. These combined studies demonstrate that the impaired energy expenditure in obesity is a function of relative fatness.

The researchers also studied independent relationships of obesity (high percentage of body fat) and overweight (high body weight) to cardiovascular risk factors, demonstrating that percent body fat rather than body weight per se is associated with increased risk. Further investigations are being conducted to establish the relative importance of other metabolic and clinical differences in obese and non-obese subjects.

National Cancer Institute

The National Cancer Institute (NCI) supports research on the causes, early detection, treatment, and prevention of digestive tract cancers.

Each year, about 151,000 Americans are diagnosed with cancers of the colon and rectum, and 62,000 die from them. These two diseases together, known as colorectal cancer, rank second only to lung cancer in cancer incidence and as the cause of cancer deaths in the United States.

Grantees Drs. James Alexander, Randall Burt, and colleagues, also at the University of Utah, studied asymptomatic patients with familial adenomatous polyposis (FAP), a rare hereditary condition in which the intestines become carpeted with hundreds of small, benign growths called polyps that can become cancerous. Individuals with FAP frequently have adenomas in a portion of the duodenum (the first part of the small intestine) that is hard to see in standard upper gastrointestinal tract examinations using an end-view endoscope, and the prevalence of adenomas in this area has not been known. The researchers found many adenomas in the area, using side-view endoscopy.

In other research, grantee Dr. Sidney Winawer at Memorial Sloan-Kettering Cancer Center in New York City and colleagues found evidence that it takes a long time, probably an average of 10 years, for the normal mucosa (lining) of the colon and rectum to transform to invasive cancer. It probably takes 5 years for the normal colon or rectum to develop adenomatous polyps, and another 5 years for the adenomas to develop into invasive cancer. Other studies have looked at the time between development of adenomas and colorectal cancer by examination of individual polyps. This study is the first to provide data on time from development of adenomas from a normal state, and the first to provide data based on colonoscopy of individuals. The findings are from the NCI-funded National Polyp Study, a multi-center, randomized controlled trial initiated in 1980. Several institutions enrolled patients into the study: Memorial Sloan-Kettering Cancer Center, Strang Clinic and Mount Sinai Hospital all in New York City; The VA Medical Center in Minneapolis, Minnesota; Medical College of Wisconsin and St. Luke's Hospital in Milwaukee and Racine, Wisconsin; Massachusetts General Hospital in Boston; Cedars-Sinai Medical Center and Valley Presbyterian Hospital in Los Angeles and Van Nuys, California.

A study suggests that dietary grain fiber intake of at least 11 grams a day may inhibit polyp development in patients with FAP. Supported by the NCI, Dr. Jerome DeCosse at the New York Hospital-Cornell Medical Center, New York City, and his associates conducted a 4-year, randomized, double-blind,

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placebo-controlled study of 58 patients with FAP. Patients assigned to a high-fiber group were given a wheat bran supplement of 22.5 grams a day while 2.2 grams a day were given to the low-fiber control group. All patients also received 4 grams of Vitamin C and 400 milligrams of Vitamin E daily. A higher percentage of patients in the high-fiber group showed polyp regression, beginning after about 6 months, than those in the low-fiber group.

NCI and DRR grantee Dr. Lisa Cannon-Albright and colleagues at the University of Utah in Salt Lake City examined a group of 670 Caucasians from 34 families whose relatives had a history of colorectal cancer or adenomatous polyps. Analysis strongly supported the dominant inheritance of a genetic susceptibility to colorectal adenomas and cancer. Further understanding of the underlying genetics requires a much larger study population. Nevertheless, the results point to the importance for close relatives of individuals with a history of colorectal cancer of having regular checkups to ensure early diagnosis. (NCI's early detection guidelines call for all individuals over age 50 to have an annual fecal occult blood test and sigmoidoscopy every 3 to 5 years.)

Researchers headed by NCI and NIGMS grantee Dr. Bert Vogelstein at Johns Hopkins University in Baltimore, Maryland discovered chromosomal changes that may contribute to the development of colorectal cancer. When surgically removed polyps and tumors of similar size and stages of development were compared, Drs. Vogelstein and Ray White at the University of Utah in Salt Lake City, and colleagues found that patients whose tumors showed the most genetic damage were most likely to develop cancer or experience a relapse. Using the extent of genetic damage as an indicator of cancer prognosis may ultimately help clinicians plan the course of therapy.

In related research, Dr. Vogelstein and colleagues identified a tumor suppressor gene--p53--that is thought to play a role in the development of colorectal cancer. Cells normally have two good copies of p53, but if both copies are damaged or lost, malignant tumors may arise. The research team included Dr. Milburn Jessup at M.D. Anderson Hospital and Dr. Peter van Tuinen at Baylor College of Medicine, both in Houston, Texas and Dr. David Barker at the University of Utah. The study was also funded by NIGMS and NICHD.

In addition, Drs. Vogelstein, Stanley Hamilton at the Johns Hopkins University and colleagues found that the extent of deletion at a particular chromosomal site was associated with metastasis (spread) of colorectal cancer and a lower survival rate.

Grantees Drs. William Schafer, Sung-Hon Kim, and colleagues at the University of California, Berkeley used

yeast mutants to discover whether high cholesterol levels can help trigger colorectal and pancreatic cancers. The researchers found that a chemical crucial to the formation of cholesterol is necessary for the functioning of a gene that is involved in the transformation of normal cells into cancerous cells. Although several epidemiologic studies have shown no increase in cancer risk among people with high cholesterol levels, the laboratory results warrant further study of the association between cancer and cholesterol. The research was also funded by NIGMS, the Department of Energy, and the National Science Foundation.

Epidemiologic research has also contributed to understanding dietary factors that may reduce risk for other digestive tract cancers. Intramural investigators Drs. William Blot, Wei-Cheng You at the Institute for Cancer Research in Beijing, China, and colleagues analyzed the eating habits of 1,700 Chinese and noted a marked reduction in the rate of stomach cancer among those who consumed large amounts of vegetables in the genus Allium, which includes garlic, onions, scallions, and chives. Stomach cancer is the most common cause of cancer death worldwide.

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National Heart Lung, and Blood Institute

Digestive disease research supported by the National Heart, Lung, and Blood Institute (NHLBI) focuses on lipid metabolism and on blood vessels and circulation of the digestive system.

Genetic Defects Leading to Elevated Triglyceride Levels and Pancreatitis Identified

Plasma triglycerides are normally removed through the action of lipoprotein lipase, an enzyme that requires for its activity the presence of the lipoprotein (a protein and fat-combining molecule designated) apoC-II. ApoC-II deficiencies are associated with markedly elevated levels of plasma triglycerides and pancreatitis (an inflammation of the pancreas, a gland that secretes various hormones and digestive enzymes).

Dr. Brian Brewer, an NHLBI intramural researcher, has studied both the apoC-II gene and the lipoprotein lipase gene to identify defects that may result in hypertriglyceridemia and recurrent pancreatitis. Dr. Brewer's studies of the apoC-II gene focused on two groups of related individuals (kindreds), one from Padova, Italy, and the other from Paris, France. In each kindred, Dr. Brewer identified a different genetic defect that led to apoC-II deficiencies and elevated triglycerides. In a kindred from Bethesda, Maryland, Dr. Brewer identified a genetic defect in the lipoprotein lipase enzyme itself. This defect, a point mutation in the lipase gene, resulted in a single amino acid substitution in the enzyme that completely inhibited its activity.

The identification of these molecular defects in patients with severe hypertriglyceridemia should provide a basis for new methods to screen patients at risk for pancreatitis and may lead to the development of specific therapies for disorders of triglyceride metabolism.

Intestinal Veins and Arteries Differ in Responses to Nerve Stimulation

Blood supplies oxygen to the digestive organs and removes and transports the products of digestion to sites elsewhere in the body. The establishment of baseline information about the normal blood supply in the digestve system is essential to any complete understanding of any diseases or disorders that may develop. Dr. David L. Kreulen, a grantee at the University of Arizona, Tucson, has studied the veins and arteries of the mesentery (a membrane that holds the intestines to the body wall), which supply blood to the intestines. He recently demonstrated that the mesenteric veins respond to nerve stimulation by contracting more than the mesenteric arteries receiving the same stimulus. Furthermore, the veins were more responsive than the arteries to certain neurotransmitters. These experiments should provide information that will be crucial in the design of drugs for digestive diseases.

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National Institute of Dental Research

The National Institute of Dental Research (NIDR) supports extensive research related to digestive disorders mainly through studies of oral sensory function, salivary gland function, and the oral phase of swallowing.

Researchers Assess Salivary Substitutes

While some causes of xerostomia (dry mouth) and its proper diagnosis have been investigated, treatment is generally still limited to a narrow spectrum of substitute fluids taken orally. Dr. Michael J. Levine, an NIDR grantee at the State University of New York at Buffalo, and his colleagues assessed several commercially available salivary substitutes for their ability to lubricate oral tissue. It has been assumed that a correlation exists between viscosity of salivary substitutes and oral lubrication, although the latter parameter has not been measured adequately. The results of Dr. Levine's studies indicate little correlation between these parameters, however, and demonstrate that salivary lubrication of oral tissues may be a more complex phenomenon than previously believed. Saliva substitutes based on carboxymethylcellulose did not appear to lubricate oral tissues well and, therefore, might not protect against potential damage to teeth and gums observed in xerostomic individuals. In contrast, the mucin-based substitute proved to be a better lubricant with values comparable to whole human saliva. Studies are under way to define the biochemical and biophysical basis of salivary lubrication and viscosity. This information may provide a rationale for developing improved substitute fluids for xerostomic patients.

A Link Between Early Malnutrition and Tooth Decay Is Shown in Humans

For the first time, researchers have shown a link in humans between early malnutrition and tooth decay, an association previously reported in animals studies. Dr. Jose O. Alvarez, an NIDR grantee at the University of Alabama at Birmingham, has been following the nutritional status and oral development of almost 200 Peruvian children since infancy. His results show that if infants suffer malnutrition in their first year, their first set of teeth is extremely susceptible to decay. Although the reason behind this finding is not yet clear, Dr. Alvarez suggests that the predisposition to decay may result from poorly mineralized tooth enamel. The research team also reports that eruption of the primary teeth of villagers who were mildly malnourished during infancy is commonly delayed by approximately 1 year; falling out of the primary teeth is delayed 2 years. Delayed development of the primary teeth might also contribute to malnourishment. If all primary teeth do not appear until age 3, it is harder to wean the child and begin solid food. These

results have important implications for assessing the role of nutrition in oral health and for comparing epidemiological data on dental caries among children worldwide.

A New System for Analyzing Oral Motor Functions Is Described

NIDR intramural scientist Dr. Anthony J. Caruso, along with NIH Clinical Center staff members Drs. Steven J. Stanhope and Douglas A. McGuire, have developed a new video-based motion analysis system for acquiring three-dimensional nonspeech movement patterns from multiple orofacial structures (upper lip, lower lip, and jaw) without restricting head motion. This technique allows researchers to noninvasively evaluate oral motor function related to the initiation of alimentation (e.g., opening and closing of the jaw and chewing motions). It can be used for evaluating function after various treatments, such as maxillo-facial surgery and dental implants.

Researchers Apply Ultrasonography to Evaluate Swallowing

In previous research, NIDR investigators in collaboration with the NIH Clinical Center Rehabilitation Medicine Department have used ultrasonography, a noninvasive procedure, to evaluate the oro-pharyngeal phases of swallowing. Recently, Drs. Jaime Brahim and Barbara Sonies applied this technique to patients undergoing reconstructive jaw surgery, a procedure that can alter oral motor performance. This technique appears to be quite useful in identifying the nature of swallowing problems in such patients and facilitates their management.

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National Institute of Neurological Disorders and Stroke

The relationship between the nervous and digestive systems is an important and complex one. In post-trauma and post-surgery patients, the leading cause of morbidity is gastrointestinal ulceration and failure of function. The National Institute of Neurological Disorders and Stroke (NINDS) supports several studies on neural control of the digestive process to learn more about how these two systems interact.

Stress Effects Monitored

It has been shown that when laboratory rats are subjected to environmental stress, such as restraint in a tube or cold temperatures, all physiological systems, including the gastrointestinal system, are disturbed. For instance, during restraint, there is increased acid secretion by the gastrointestinal tract. NINDS grantee Dr. Richard C. Rogers of Ohio State University is investigating the effects of stress on the gastrointestinal system and how the brain controls motility, acid secretions, and function in the intestine of laboratory rats. Using advanced techniques, Dr. Rogers monitors gastric motor function, measures gastric acid secretions, and determines the effects of central nervous system activities. He has established that the brain hormone oxytocin plays a significant role in the digestive tracts gastric acid secretion and motility. This information may lead to more effective ways of managing stress-induced gastric pathology.

The Botulin Neurotoxin: Toxicity and Utility

Botulin food poisoning causes vomiting, abdominal pain, vision problems, central nervous system symptoms, motor disturbances, and other difficulties. The NINDS is supporting a number of studies on botulin toxin focusing both on the mechanism of toxicity and the potential utility of this toxin in the treatment of other disorders.

It is thought that the amino acids making up this toxin may alter themselves, creating new strains through mutation. Up until the mid-1960's, only five (A-E) of the seven types of the botulin neurotoxin were known. In the 1970's, strains F and G of the botulin neurotoxin were discovered. At the present time, when a person contracts botulism, the first line of treatment is an injection of a "shotgun" serum, which acts on all seven strains, followed by a "bullet" injection that works on one specific strain, once it has been identified as the toxin.

NINDS grantee Dr. Bibhuti R. DasGupta of the University of Wisconsin at Madison is attempting to unlock the mysteries of the structure and mechanism of botulin toxicity. His work

focuses on finding out which ingredients are common to each of the seven strains and would allow them to be treated by one serum, and which ingredients are different and would require different serums. Dr. DasGupta has identified some of the sequences of the 1,300 amino acids that comprise the structure of the botulin neurotoxin, and hopes that the sequencing of the entire structure will lead to a serum for the next strain when the neurotoxin mutates again.

Grantee Dr. Lance Simpson of the Thomas Jefferson University in Philadelphia, Pennsylvania is studying the mechanism of action in the botulin neurotoxin. Using mice and tissue samples, he hopes to use the toxin itself, or a modified version of the toxin, as a therapeutic agent. Because there are instances where it is advantageous to use a toxin to block transmitters in neurological disorders, the botulin toxin may prove promising as a therapeutic agent. Dr. Simpson's pharmacological findings, thus far, suggest one type of tumor tissue in mice where a botulin toxin is a suitable tool.

Regulation of the Pancreas

At Columbia University in New York, grantee Dr. Annette Kirschgessner is investigating enteric (intestinal) innervation and regulation of the pancreas. Previously, it was thought that regulation of the pancreas was hormonal. Dr. Kirchgessner has determined that there is also a neural innervation. She has found the presence in the pancreas of the neurotransmitter serotonin and hopes to discover what its role is. Additionally, Dr. Kirchgessner is concerned with what stimuli act on this neural pathway.

How Stroke Affects Swallowing

With NINDS support, Dr. Joanne Robbins of the University of Wisconsin at Madison is investigating the effects of stroke and its location in the brain on swallowing. Her study entails sophisticated computer measurements of duration between the swallowing command, its initiation, beginning of tongue movement, and throat and pharynx involvement. She and her colleagues have studied about 70 patients--one-third with strokes on the left side of the brain, one-third with strokes on the right, and one-third normal controls.

Findings vary according to the location of the primary impairment. For example, right cortical stroke patients have swallowing difficulties characterized by aspiration or material moving into the air passage. In left cortical stroke patients, there were orally-based movement problems, such as difficulties with tongue movement. Dr. Robbins' laboratory is also studying patients with subcortical strokes and brainstem strokes to compare the swallowing effects of those stroke locations with the effects of strokes in other brain areas.

National Institute of Allergy and Infectious Diseases

Diarrheal diseases and viral hepatitis are major causes of morbidity and mortality worldwide. The National Institute of Allergy and Infectious Diseases (NIAID) has had a long-standing interest in these problems because they are caused by infectious agents and have a widespread impact on human health.

Experimental Concentrate Prevents Travelers' Diarrhea

In a controlled clinical trial, NIAID contractors found that a concentrate of infection-fighting proteins taken from cows' milk completely prevented travelers' diarrhea and caused no adverse side effects in 10 human volunteers. The research was carried out by Dr. Carol O. Tacket and coworkers at the University of Maryland School of Medicine's Center for Vaccine Development in Baltimore.

Between 30 and 50 percent of all Americans who travel to developing countries contract travelers' diarrhea. Numerous infectious organisms can cause the illness, but the most common culprit is enterotoxigenic Escherichia coli (ETEC), a harmful form of the normally helpful E. Coli bacterium found in the gut.

The concentrate used in the study was taken from nursing cows that had been immunized during gestation with various types of ETEC and one form of ETEC toxin. The expectation was that immunizing cows with this concoction would stimulate production of antibodies to the variety of antigens found on the surfaces of the bacteria and the toxin. Antibodies were produced as expected, and these were isolated from the milk and dried into a powder.

In the experiment, volunteers mixed the dried material with water and drank it for several days before being challenged with ETEC. A control group of 10 volunteers received a similar-looking concentrate, followed the same regimen, and were not protected. However the antibodies introduced from the concentrate effectively prevented volunteers from developing ETEC-caused diarrhea. In addition, the anti-ETEC concentrate promoted some degree of antibody production by the volunteers' own immune systems. This latter type of immunity, called active immunity, can provide many years of protection against an organism.

Basic Understanding of Immune Response to Hepatitis B May Lead To Improve Synthetic Vaccine

NIAID grantee Dr. David R. Milich, of the Research Institute of Scripps Clinic in La Jolla, California, and his coworkers have conducted experiments in mice that may lead to improved synthetic vaccines for hepatitis B as well as other

diseases. They have found that to be most effective, such vaccines must include two different parts of the virus as immunogens (substances that induce an immune response), those that bind T cells as well as those that bind B cells. (T and B cells are the two main classes of immune system cells.) Many synthetic vaccines now in development, including the currently proposed synthetic hepatitis B virus vaccine, have been constructed with B-cell sites only. Scientists think that including T-cell sites in synthetic vaccines will improve the response rate to these vaccines.

About 15 percent of people do not respond to the currently licensed hepatitis B virus vaccine. In their work with mice, Dr. Milich and coworkers found that a certain strain of mice that was unresponsive to a hepatitis B immunogen containing only B-cell sites did respond to the immunogen when T cells sites were added. Their experiments provide the first model of how to overcome non-responsiveness in human vacinees.

T-cell sites are thought to be important because they stimulate the production of memory T cells that induce long-term antibody production by B cells. Memory T cells allow a quicker, stronger immune response to develop upon second exposure to a particular virus or other antigen.

This experimental model developed by Milich and coworkers can now be used to study the genetic, cellular, and molecular basis for the variable human response to vaccines, and provides a framework for the design of second- and third-generation HBV vaccines.

New Understanding of Hepatitis Delta Virus Replication Achieved

Hepatitis delta virus (HDV) can cause a severe, fulminant form of hepatitis that most often leads to death. HDV is always found together with hepatitis B because HDV is a defective virus that cannot replicate by itself. HDV commonly affects intravenous drug users since many are already infected with hepatitis B.

NIAID-supported grantee Dr. Michael M.C. Lai at the University of Southern California in Los Angeles in collaboration with a Taiwanese researcher, has made an extremely important discovery about HDV. They have found that the genetic material of HDV, a circular-shaped ribonucleic acid (RNA), does not just passively carry genetic information but also actively directs certain biochemical activities of the virus. Because of these qualities, HDV RNA can be placed in a new class of RNAs, called catalytic RNAs or ribozymes.

The 1989 Nobel Prize in chemistry was awarded to NIH grantees for their discovery that such a class of RNAs

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exist. A ribozyme acts like an enzyme; it can cleave itself and likewise mend, or ligate, such breaks. This cleavage and ligation activity is required for the virus to replicate. The HDV RNA is a member of a class of newly identified ribozymes.

This discovery that HDV is a ribozyme has profound implications for the development of drugs to arrest infection with the virus. The site on HDV where self-cleavage occurs has a very specific, three-dimensional structure. One goal is to find a drug or drugs that can bind to this site, and thus interrupt HDV replication. On the other hand, the ribozyme itself potentially can be developed into a tool to inhibit the expression of other important genes. Because HDV also inhibits hepatitis B virus replication, this new understanding of the virus may also be applied to the development of therapies for hepatitis B.

National Institute of General Medical Sciences

Among the research supported by the National Institute of General Medical Sciences (NIGMS) aimed at understanding and treating digestive diseases is the work of Dr. David R. Friend at SRI International in Menlo Park, California. He and his colleagues have designed a series of compounds that may prove useful in the site-specific treatment of inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis.

IBD is a chronic disease that affects millions of people worldwide. Doctors can prescribe a number of drugs to treat the condition, but, in addition to having unwanted side effects, these drugs are also difficult to direct specifically to the colon.

Dr. Friend's group has developed a clever scheme to get powerful anti-inflammatory drugs to the colon while insulating the rest of the digestive tract from the chemicals. The drug molecule is attached to some other molecule, such as a sugar. The resulting compound, called a prodrug, is given orally. The prodrug is not easily absorbed by the stomach or small intestine. However, when the prodrug reaches the colon, it comes in contact with enzymes produced by the microoganisms that live in that part of the gut. (These micoorganisms are not prevalent higher in the digestive tract.) The enzymes clip the sugar molecule off the prodrug, liberating the active drug, which is then absorbed by the colon. The enzymatic activity in the colon can be increased by encouraging the growth of microorganisms through a high-fiber diet. Thus, in theory, this approach not only permits site-specific delivery of a drug, it also allows for adjustments in the rate of drug release.

Currently, Dr. Friend is conducting tests in animals to determine how well the various prodrugs he has designed are delivered, converted to active drugs internally, and absorbed. He has used guinea pigs because the distribution of gut microorganisms in guinea pigs is similar to that in humans. His early results indicate that the prodrugs are successfully converted to the active drugs when they reach the colon.

In addition to funding research in the pharmacological sciences, as exemplified by Dr. Friend's studies, NIGMS also supports studies in such fundamental biomedical disciplines as genetics, cellular and molecular biology, biophysics, and physiology. Findings in these areas often yield important insights into the mechanisms of disease, including digestive disorders.

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National Institute of Child Health and Human Development

The National Institute of Child Health and Human Development (NICHD) has conducted or supported studies in digestive diseases to gain insight into the complex process of digestive tract development and to develop methods for the prevention and treatment of digestive disorders in infants and children.

Hirschsprung's Disease

A recent NICHD study conducted at Columbia University College of Physicians and Surgeons yielded information that can be applied to examining the origins of Hirschsprung's disease, in which the lower portion of the bowel is enlarged due to the absence of functional nerve distribution. Furthermore, this experimental information may also help in the development of possible therapies for the disease.

Using the lethal spotted (ls) mouse as an animal model, Dr. Virginia Tennyson and her coworkers demonstrated that cells orginating from the developing central nervous system migrate to the intestinal wall where they become concentrated into masses of nerve cells, or ganglia. Along their journey, these "neural crest cells" encounter various guidance cues, including individual components of the extracellular matrix (i.e., the foundation on which cells are based), as well as different cell types.

Using techniques to introduce genetically marked neural crest cells into experimental animals, the researchers demonstrated that normal neural crest cells are unable to develop in the bowel of ls mice, while neural crest cells from the defective strain can develop into ganglia in a normal intestine. This indicates that the intestinal matrix, not the cells, gives rise to the developmental defect.

In the mutant animal the terminal portion of the colon was found to have abnormally high levels of laminin, a normal component of the extracellular matrix. Low levels of this component were found in previous studies to promote neural crest cell migration, while high levels appear to inhibit migration. The high levels of laminin in the mutant animals appear to interfere with the migration of neural crest cells and their development in the bowel, leading to the abnormal bowel enlargement.

Shigellosis

Although the benefits of breast-feeding are well known, less is understood about how these benefits are derived. For example, breast-feeding appears to protect infants from diarrheal disease due to shigella organisms (which cause acute bowel infection) but how it protects them remains unclear.

National Institute of Environmental Health Sciences

There is considerable evidence from both animal and human studies that environmental agents contribute to the development of digestive diseases. Because the digestive and metabolic processes are central in the activation and inactivation of environmental chemicals, one of the cornerstones of modern toxicology is the examination of liver and other digestive system organs in laboratory animals exposed to these chemicals. Thus, the National Institute of Environmental Health Sciences (NIEHS) supports a variety of studies examining the direct effects of environmental chemicals on the metabolic and digestive processes and the mechanism for the action of the chemicals or their metabolites on these systems.

Metabolic Enzymes

Mammalian cells possess a remarkable family of enzymes, the cytochrome P450s, which catalyze a variety of important reactions involved in the conversion of organic molecules to compounds that can be either utilized by the body or excreted. These P450-mediated reactions, although essential for life, also are often responsible for the conversion of foreign chemicals to toxic products within the body. NIEHS grantees have made significant progress in the past year towards understanding the ways in which these enzymes catalyze environmental chemical conversion.

The presence of a variety of P450 enzymes in cells has been demonstrated, but most of the animal models remain poorly characterized in terms of which specific P450's are involved in an individual biotransformation reaction. It is important to identify these enzymes in order to understand how the cell changes some chemicals to toxic products. NIEHS grantee Dr. James Halpert and others at the University of Arizona in Tucson have designed a selective agent to inactivate one P450 enzyme responsible for progesterone hydroxylation, a normal physiologic reaction that occurs. This technique is now being refined to develop tools for probing and modulating the function of individual cytochrome P450's involved in the metabolism of chemicals. Such studies are valuable because they could be used to develop agricultural and industrial chemicals that would not be converted internally to toxic products by human cells and, therefore, would be safer to use.

Activation of chemical metabolizing enzymes, which results from increasing the concentration of the enzyme in the cell (induction), might sometimes result in an enhanced predisposition to toxicity. NIEHS grantee Dr. Raymond Novak and colleagues at Wayne State University in Detroit have examined the potential of a widely used industrial compound, pyridine, to affect the P450 enzymes. (This compound and a variety of pyridine-based compounds are widely employed in the

Genetic information conferring virulence (ability to invade cells and cause disease) on the shigella bacterium is coded in two places: on the bacterium's chromosome and on plasmids, which are separate, self-replicating pieces of genetic material exchanged among different bacteria. An antibody to a virulence determinant carried on the chromosome is present for a short time in breast milk, but does not explain protection throughout lactation.

A group led by Dr. Thomas Cleary at the University of Texas Medical School in Houston has looked for antibodies (called sIgA) to specific antigens in breast milk and colostrum, the thin, milky fluid secreted by the mammary glands for several days after childbirth. Milk samples were taken from women in Mexico City, where there is a high rate of shigellosis, as well as from women in Houston where the infection is relatively uncommon. One hundred percent of the milk samples from the women in Houston had sIga to the plasmid-coded antigens involved in shigella invasion of mammalian cells.

From this research, it appears that the antibodies to the shigella antigens coded on the bacterial plasmids afford the protection provided to infants by human milk.

Allergic Reactions to Breast Milk Proteins

Despite the benefits of breast-feeding, infants sometimes develop untoward reactions such as colic, dermatitis, and colitis in response to specific proteins in the mother's diet.

The transfer of a protein antigen from the lactating mother to the infant involves a complex process in which the ingested protein passes through the intestine undigested and penetrates the gastrointestinal barrier. The protein then travels through the general circulatory system without being eliminated before reaching the mammary gland, and is finally transferred to the milk.

To study this process, Dr. Alan Walker and his colleagues at the Massachusetts General Hospital developed a mouse model using the protein ovalbumin as the test antigen. They found that the uptake of the protein was eight times greater in lactating animals than in non-lactating control animals.

Further studies indicated that at least two variables contribute to this enhanced uptake: 1) prolonged contact of the protein with parts of the intestine that may be capable of increased uptake; and 2) an increased association of the protein with the intestinal surface. These findings should help provide clues to the mechanisms behind some of the allergic reactions in breast-fed infants.

pharmaceutical and chemical industries as solvents or intermediates in the production of therapeutic agents, pesticides, and rubber products. The annual production of these compounds is over 2 million pounds and the worker population exposed to pyridine is in excess of 33,000). These researchers have shown, through inhalation exposure of rats, that pyridine is a potent inducer of certain P450 enzymes that are active in the metabolism of a variety of toxic agents including nitrosamines. Since the toxicity of many chemicals such as the nitrosamines is the result of biotransformation by P450 enzymes, increasing the concentration of these enzymes can increase the susceptibility of animals and humans to such chemicals.

The activation of chemical-metabolizing enzymes may also affect the toxicity of commonly used therapeutic agents because many of these compounds are acted upon by the same group of enzymes. For example, Mirex, an organochlorine pesticide formerly used in the southeastern United States for the control of fire ants, is a potential health threat because it is stored in fatty tissue, and is likely to accumulate in animal fat due to the lack of its significant metabolism in vertebrate animals. However, this pesticide has also been reported to increase the amount of liver cytochrome P450 enzymes, raising questions as to the effect of Mirex exposure on the toxicology of therapeutic drugs that are also metabolized by the P450 enzymes. At North Carolina State University in Raleigh, NIEHS grantee Dr. Ernest Hodgson and others have shown that exposure of mice to Mirex increased the liver toxicity of the widely used analgesic, acetaminophen. Data from these initial studies, which suggest that exposure to organochlorine pesticides can potentiate the liver toxicity of medicines, must be considered when assessing the toxicity of therapeutic compounds.

Aged More Vulnerable to Toxic Chemicals

The aged may represent a population at special risk for toxic insult. Current research by NIEHS intramural scientist Dr. Linda S. Birnbaum and her colleagues is focusing on the effect of aging on absorption and metabolism of toxic chemicals. Using rats and mice from 3 to 30 months of age, these workers found that active absorption of chemicals from the GI tract decreased with age while passive absorption remained unchanged. Dermal absorption of chemicals declines with age, but this does not appear to be due to changes in skin structure or blood flow. Distribution of chemicals alters as lean body mass and plasma protein binding decrease. Elimination of chemicals decreases with age due to alterations in renal physiology and gallbladder function. Salicylate, the active compound in aspirin, is more toxic to the kidneys of older organisms. Old rats produce more of the toxic metabolite of aspirin than do young rats. The toxicity of this metabolite can be studied nonivasively by measuring

urinary enzymes shortly after treatment. Old mice also show enhanced sensitivity to cyanide intoxication. This may be due, at least in part, to a decline in the activity of rhodanase (an enzyme which detoxifies cyanide) in the aging brain. These studies demonstrate alterations in chemical metabolism resulting in enhanced toxic sensitivity in the aged. Future studies will explore the relationship between age-related changes in benzene sensitivity and pharmacokinetics.

National Institute On Aging

The National Institute on Aging (NIA) supports a number of studies on digestive diseases and disorders--one of the primary causes of hospital admissions for older people. The Institute has developed a research focus on nutrition that includes a study on the way aging affects the intestine's ability to absorb nutrients.

Study Shows Age-Related Reduction In Nutrient Absorption

According to a study using animal models of aging, conducted by Dr. Peter R. Holt at Columbia University and St. Luke's Roosevelt Hospital Center, in New York City, certain age-related changes take place in the intestine that may make it difficult to adequately absorb various nutrients. The investigators looked at the small intestines of old rats (27 to 28 months old) and young rats (4 to 5 months old) under normal dietary conditions and after starvation and re-feeding. They found sharply reduced levels of enzyme activity in the intestine of older rats, both under normal conditions and especially after starvation, when compared to the younger rats. Intestinal enzymes play a vital role in ensuring nutrients are absorbed efficiently. In addition, the small intestine and colon of older rats show cellular changes with the stress of starvation and refeeding that resemble well established, pre-malignant colonic conditions.

Changes in intestinal absorption may increase the risk for some diseases or illnesses. Weight loss and malnutrition often occur after an illness or surgery, and nutrients must be restored to return the body to normal health. The intestine of the older patient may not respond adequately to ensure such nutrient restoration.

Osteoporosis, one of the most common disorders associated with aging, may be exacerbated by a decline in calcium absorption, associated with nutrient malabsorption. Pernicious anemia, a condition marked by a deficiency of vitamin B12, can also result. Hypochlorhydria (a deficiency of hydrochloric acid in the stomach), another syndrome that appears to increase with age, is also characterized by a decreased absorption of vitamin B12.

The researchers recommend increased research on digestive diseases in older people and cite the need to develop a non-invasive test to measure intestinal absorption and malabsorption of a variety of substances.

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Division of Research Resources

The Division of Research Resources (DRR) supports and conducts research into a large number of gastrointestinal disorders at shared resource centers across the United States. These disorders are among the most difficult to diagnose correctly. Symptoms, such as abdominal pain and bloating, or an abnormal frequency of bowel movements, are not easily linked to a specific condition.

Intestinal and stomach blockages that pose a serious threat are hard to differentiate from a benign condition called aerophagia, also known as air swallowing. Expensive and invasive procedures are usually required to diagnose this relatively harmless condition. But a new medical device developed and tested by DRR grantees may enable physicians to identify aerophagia easily and inexpensively.

The device developed by Dr. William Whitehead at the Francis Scott Key Hospital General Clinical Research Center in Baltimore, Maryland records swallowing patterns. Sensors measure the movement of tongue muscles and transmit signals to a small, battery-operated monitor. Movement caused by swallowing is identified and logged along with the time that the swallowing occurred.

The investigators believe these records will help them identify the specific pattern of swallowing that defines aerophagia. Preliminary data indicate that the condition is often present in people who swallow throughout the day, even when they are not eating or drinking, and in people who snack frequently and take a long time to eat. It is believed that these habits cause symptoms of bloating, pain, and belching by carrying excessive amounts of air to the small intestine and colon.

Diagnosis of aerophagia with the swallow monitor will, in some cases, eliminate the need for more invasive diagnostic techniques. According to Dr. Whitehead, each use of the device would cost only about $300, as opposed to $500 to $1,000 for a procedure in which the physician looks at the inside of the stomach or colon through a flexible tube called an endoscope. Feedback from the monitor may also help patients track and modify their swallowing patterns to remedy aerophagia.

Some digestive diseases require more intensive therapy. Patients with an inherited disorder known as Hartnup disease have a defect in the cells that line the inside of the gastrointestinal tract. This defect, which prevents absorption of an amino acid called tryptophan, can result in severe diarrhea, skin rashes, growth failure, developmental delay, and episodes of ataxia, a condition in which the patient is unable to walk normally.

DRR grantee Dr. Adam J. Jonas at the Harbor-UCLA Medical Center in Torrance, California found that tryptophan, when chemically modified, can be absorbed despite this defect. Dr. Jonas has been using the modified tryptophan in laboratory studies conducted at the University of Texas Health Science Center in Houston to examine the mechanisms by which molecules are transported across cell membranes. He then began a study at the University of Texas Health Science Center GCRC to determine its effect on a patient with tryptophan deficiency due to Hartnup disease. When Dr. Jonas moved to the Harbor-UCLA Medical Center, the GCRC research staff continued the study, sending samples to Dr. Jonas for analysis.

During the one year of treatment with modified tryptophan, the patient with Hartnup disease resumed normal growth. No toxicity has been observed from use of the formulation. The diarrhea and skin rashes, which had been symptomatic of the disease, are no longer present.

According to Dr. Jonas, this application must be tested on more Hartnup patients to determine its effectiveness. Some patients, he notes, may need amino acids other than just tryptophan.

Dr. Jonas believes that other amino acids might be similarly modified into more easily absorbable formulations. If so, these formulations might provide effective and simple ways to treat a variety of diseases caused by amino acid malabsorption.

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Outlook

The many developments and advances described in this report demonstrate the progress being made against digestive diseases through research by grant-supported and intramural scientists of NIH. This effort, led by NIDDK, will continue to focus on a coordinated program of basic and clinical research into the normal function and the diseases of digestion. In the coming years, prevention will play an ever-increasing role in NIH's research programs in this field.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
REPORT ON POPULATION AND FAMILY PLANNING ACTIVITIES

A REPORT TO THE
HOUSE COMMITTEE ON APPROPRIATIONS

Prepared by
The Office of Population Affairs
February 1990

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I

INTRODUCTION

This report describes the population research, family planning and population education activities of the Department of Health and Human Services.

Population research and family planning activities in the Department of Health and Human Services include support of service--making family planning information and services available and accessible; training--meeting the professional and lay manpower needs in health, social services, and education; research--promoting and supporting research and research training in the biomedical and broad behavioral aspects of fertility, sterility, population dynamics, and program implementation, and public education--increasing opportunities for public understanding of human sexuality, population education and information about family planning.

Under the Social Security Amendments of 1967 (Pub. L. 90-248), subsidized family planning services were made available through a variety of sources to some of those who want but cannot afford them. The Social Security Amendments of 1972 (Pub. L. 92-603) required that family planning services be offered and provided promptly upon request to all recipients of Aid to Families with Dependent Children (AFDC) and of medical assistance (Medicaid). The Social Services Amendments of 1974 (Pub. L. 93-647) added a Title XX[1] to the Social Security Act (SSA). Under the Social Services Amendments of 1976 (Pub. L. 94-401), States had the option of providing family planning services under Title XX to individuals regardless of their income. The major provisions of Pub. L. 92-603 continued in effect until Title XX was amended by Pub. L. 97-35, establishing the social services block grant program effective October 1, 1981[2].

The Family Planning Services and Population Research Act of 1970 (Pub. L. 91-572) established Title X of the Public Health Service Act, the major direct source of Federal support for family planning services programs.

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[1] As initially enacted, SSA Title XX applied to the 50 States and the District of Columbia. Family planning social services for Guam, Puerto Rico, and the Virgin Islands were available under SSA Titles I, IV, X, XIV, and XVI.

[2] The participants in the Title XX social services block grant program are the 50 States, the District of Columbia, Guam, Puerto Rico, the Virgin Islands and the Commonwealth of the Northern Mariana Islands.

Legislative Highlights

1. On January 2, 1968, the Social Security Amendments of 1967 (Pub. L. 90-248), which included the Child Health Act of 1967, were enacted. This Act established categorical project grants for family planning services and required that not less than six percent of the monies appropriated for Maternal and Child Health under SSA Title V be available for family planning services. This same legislation required that under SSA Title VI-A, the AFDC program, family planning services were to be offered in all appropriate cases. Acceptance of such services was voluntary.

2. On December 24, 1970, the Family Planning Services and Population Research Act of 1970 (Pub. L. 91-572) was enacted, establishing Title X of the Public Health Service Act. This Act was passed to assist in making comprehensive voluntary family planning services available to all persons desiring such services.

3. Title X funding authorizations were extended by Pub. L. 93-45 in 1973, Pub. L. 94-63 in 1975, Pub. L. 95-83 in 1977, Pub. L. 95-613 in 1978, Pub. L. 97-35 in 1981 and Pub. L. 98-512 in 1985.

4. On October 30, 1972, the Social Security Amendments of 1972 (Pub. L. 92-603) were enacted. This Act made it mandatory to inform all recipients of AFDC of the availability of family planning services and to provide or contract for services to all eligible persons voluntarily desiring them. This Act imposes a penalty of one per cent per anum on the Federal share of AFDC funds on States which fail to provide them to eligible persons desiring them. In addition, the Act increases the Federal share of matching for family planning services under Title VI-A--AFDC--to 90 percent from 35 percent. It also made family planning services a required service for all Title XIX--Medicaid--programs, subject to a 90 percent Federal matching rate.

5. On January 4, 1975, the Social Services Amendments of 1974 (Pub. L. 93-647) were enacted. These Amendments established SSA Title XX which placed major responsibility upon the States to develop their social services programs to be responsive to the needs of the citizens of each State. Title XX continued the requirement under Pub. L. 92-603 that family planning services be offered and provided promptly to those AFDC recipients requesting such services. States had the option of providing family planning services on the basis of income eligibility status. In addition, States were required to provide three services to recipients of Supplemental Security Income (SSI) payments to the aged, blind and disabled. Family planning could have been one such service. The Federal share of matching was at the 90 percent rate.

6. On September 7, 1976, Pub. L. 94-401 amended SSA Title XX, adding a provision that States may provide family planning services to individuals regardless of their income.

7. On November 10, 1978, the Health Services and Centers Amendments of 1978 were enacted. This Act established under Titles VI, VII and VIII within the Office of the Assistant Secretary for Health and in consultation and coordination with the Deputy Assistant Secretary for Population Affairs, programs to prevent or reduce unwanted and repeat pregnancies among adolescents. These programs were to enable pregnant adolescents to obtain proper care and to become productive independent contributors to family and community life. In 1981, this program was incorporated into the Maternal and Child Health Block Grant.

8. On August 13, 1981, Congress amended Title XX of the Social Security Act by enacting social services block grant legislation under Pub. L. 97-35. This block grant legislation became effective October 1, 1981. States were given greater flexibility in administering their social service programs than they had under the previous Title XX programs. Any requirements with regard to eligibility for services and what services to cover are now left to the discretion of the States.

SUMMARY OF DHHS PROGRAM ACTIVITIES BY OPERATING AGENCY

PUBLIC HEALTH SERVICE

Office of the Assistant Secretary for Health

Office of Population Affairs

Supports delivery of family planning medical services, counseling and referral.

Supports short-term training for family planning professional health personal.

Supports family planning information and education activities.

Supports social research in the area of family planning service delivery.

Office of International Health

Policy development and coordination for international health program and activities.

National Institutes of Health

National Institute of Child Health and Human Development

Supports basic biomedical research on reproductive physiology and contraceptive development.

Supports social research on the causes and consequences of population structure and change, including factors affecting fertility and family planning.

Food and Drug Administration

Sponsors and monitors research on contraceptive safety.

Maintains a contraceptive reporting system.

Health Resources and Services Administration

Bureau of Health Care Delivery Assistance

Supports family planning services as well as consultation and technical assistance.

Bureau of Health Professions

Supports professional education programs for physicians and nurses.

Supports Family Nursing research.

Indian Health Service

Provides family planning information and education services.

Centers for Disease Control

Center for Chronic Disease Prevention and Health Promotion

Conducts epidemiologic field investigations of contraceptive methods and analysis of pregnancy-related morbidity and mortality.

Provides training for health professionals.

National Center for Health Statistics

Conducts social research on fertility, family planning, and the reproductive health of American women.

OFFICE OF HUMAN DEVELOPMENT

Office of Policy, Planning and Legislation

Supports family planning services, including counseling and information and referral services through the Social Services Block Grant. Also supports social services projects and evaluations that address teen pregnancy prevention.

SOCIAL SECURITY ADMINISTRATION

Health Care Financing Administration

Bureau of Program Operations
Provides family planning services and supplies including sterilization services, to categorically needy persons through the Medicaid program.

II

PUBLIC HEALTH SERVICE

Office of the Assistant Secretary for Health

Office of Population Affairs

The Office of Population Affairs (OPA), under the direction of the Deputy Assistant Secretary for Population Affairs (DASPA), administers the Title X Family Planning Program and the Title XX Adolescent Family Life Program. In addition to these program administration activities, the DASPA advises the Secretary, through the Assistant Secretary, on policy and new legislation; participates in legislative and fiscal planning; and prepares reports on departmental and inter-departmental activities for the Secretary and the Congress. The DASPA also works in cooperation with other Federal agencies, as well as with other concerned organizations, in the areas of population research and family planning services, training and education.

Within the OPA, the Office of Family Planning administers family planning activities authorized under the "Family Planning Services and Population Research Act of 1970" (P.L. 91-572), which established Title X of the Public Health Service Act. Title X authorizes project grants for voluntary family planning services, and grants and contracts for continuing professional education for family planning services personnel, for service delivery improvement research, and for family planning information and education. Categorical project grants under Title X of the PHS Act represent the major Federal source of direct funding for family planning services.

The broad purposes of Title X are stated in the law as follows:

1. To assist in making comprehensive voluntary family planning services readily available to all persons desiring such services;

2. To improve administrative and operational supervision of family planning services;

3. To enable public and nonprofit private entities to plan and develop comprehensive programs for family planning services;

4. To develop and make readily available information (including educational materials) on family planning to those desiring such information;

5. To evaluate and improve the effectiveness of family planning service programs; and

6. To assist in providing trained personnel needed to carry out family planning programs.

The primary target group for Title X family planning services is the estimated 8.4 million low income women of childbearing age. More than 4 million of these women receive services from organized family planning--3.6 million from Title X funded programs. Another 2 million receive services from private physicians.

The Office of Family Planning allocates Title X service funds to the ten DHHS regional offices, which in turn allocate these funds among their 86 grantees, request and approve applications for Title X service grants, and monitor grantee performance. A Regional Program Consultant for Family Planning serves as coordinator for family planning activities in each Region. Title X currently funds about 4,000 family planning clinics throughout the United States and its territories.

The primary objectives of the program have been to continue to provide high quality family planning services, to improve the efficiency and effectiveness of family planning projects, and to encourage the involvement of the family in the provision of family planning services. Staff development programs, information and education activities, and service delivery improvement research have been directed to support the attainment of these objectives.

Title X training programs are designed to provide personnel with the skills and knowledge and necessary for the effective delivery of family planning services. Training is provided in structured and non-structured settings and includes in-service education, staff development, and continuing education activities that are innovative, self-paced, self-instructional or mediated with newer technological advancements in the field of education. The current national training priority areas are 1) clinic management, 2) counseling and client education, 3) family involvement, 4) management of infertility, including adoption, 5) natural family planning (NFP), 6) program management, 7) prevention of sexually transmitted diseases (STDs), including HIV infection and AIDS, 8) adolescent abstinence from premarital sexual activity, and 9) male involvement.

In Fiscal Year 1989, ten general training grants, one in each of the DHHS regions, were awarded. These grants are aimed at providing training for all personnel who are employed in Title X funded clinics such as managers, mid-level providers, professional and technical staff and clerical/receptionist staff.

The five obstetric/gynecology or women's health care nurse practitioner programs are specifically designed for registered professional nurses who are employed in family planning clinics to become nurse practitioners. Approximately 142 nurse practitioners completed programs for Title X clinics in Fiscal Year 1989. Nurse practitioners provide 60-70 percent of all encounters in family planning clinics. They are an essential part of the family planning services delivery system because they increase a clinic's capacity for providing high quality, cost-effective health care services to more clients. All Title X funded nurse practitioner programs are nationally accredited by the American Nurses' Association. Since the beginning of the training program in 1973, Title X funded training projects have produced more than 2,796 nurse practitioners. All of the general training grantees were provided with supplemental awards to support training activities on HIV/AIDS.

The major activities supported under the Title X information and education program include the operation of the National Clearinghouse for Family Planning Information and the development of information and education materials for family planning clients and clinic staff. During FY 1989, the Clearinghouse distributed over 500,000 pieces of educational or informational material including patient education pamphlets, information and education bulletins for clinic staff and bibliographies. Prominent among these materials was a guidebook entitled The Adoption Option developed by OPA for pregnancy counselors and a booklet, "Adolescent Abstinence", which was developed by the Association of State Family Planning Administrators with funding from the OPA. A new brochure, "Your Contraceptive Choices For Now, For Later", was also developed and distributed. Because of its usefulness in discouraging premarital adolescent sexual relations and the number of requests, the pamphlet, "Many Teens are Saying "NO", was again reprinted. Additionally a Spanish language version of this pamphlet was developed and printed.

The focus of the Service Delivery Improvement (SDI) Program continues to be enhancement of the delivery system, particularly at the clinic level. In addition to direct technical assistance efforts in this regard, the SDI research program funded projects to obtain knowledge needed by family planning service providers to better understand service delivery processes and how such processes may be influenced in the desired direction. Three continuation research grants were supported, covering an array of topics--male involvement in family planning, the utility of a computerized counseling aid, and the effects on service provision of integrating family planning services and sexually transmitted disease services. A SDI research contract was also awarded to make available computer readable data on family planning in the form of a data archive.

INTERNATIONAL ACTIVITIES

The Office of International Health (OIH), a staff office to the Assistant Secretary for Health, has primary responsibility in the Public Health Service for overall policy guidance and coordination of PHS international health programs and activities, on behalf of the Assistant Secretary for Health. OIH assures that policy issues related to population and family planning are appropriately addressed in the governing bodies of multilateral organizations (e.g. the World Health Organization and the United Nations Children's Fund), and it promotes involvement in activities of those agencies throughout the year. OIH also promotes cooperation with other countries through a variety of U.S. bilateral agreements. Involvement of the PHS in implementing selected aspects of the U.S. foreign assistance program through the Agency for International Development has been an integral part of the PHS international programs for over two decades.

At the United Nations Children's Fund (UNICEF) Executive Board Meeting in April 1989, the U.S. Delegation encouraged UNICEF to place greater emphasis on child spacing. PHS personnel serve on numerous Steering Committees and Task Forces of the World Health Organization, including such groups as the Task Force on Male Methods of Fertility Regulation, the Task Force on Post-Ovulatory Drugs, and the Task Force on Vaccines for Fertility Regulation. Cooperative and collaborative efforts have continued with the World Health Organization regarding the development of safe and efficacious methods of fertility regulation and other population-related issues. For example the National Institute of Child Health and Human Development (NICHD) has undertaken extensive screening of chemicals synthesized by WHO. In turn, WHO has done some of the clinical testing of contraceptive products developed either by the Institute alone or through joint funding.

PHS bilateral cooperation in the areas of population and family planning has continued with India and the People's Republic of China (PRC). Scientific information, experimental reagents, antisera, standards, and radioimmunoassay kits have been exchanged previously with Chinese scientists as a result of discussions and visits to the PRC by staff of the Center for Population Research (CPR), NICHD. Interaction by CPR staff with visiting Chinese scientists concerning research in reproductive biology and contraception has continued.

Collaboration on reproductive and contraceptive research beteween NICHD and the Indian Council of Medical Research (ICMR) has continued, both under the auspices of the Indo-U.S. Subcommission on Science and Technology and as part of the Gandhi-Reagan Science and Technology Initiative. NICHD and the ICMR jointly sponsored the sixth Indo-U.S. Workshop on Reproduction and Contraceptive Research, which was held in November 1988 in Bethesda, Maryland. The Workshop was held in order to review past progress and ongoing efforts and to discuss potential new areas for collaboration. The topics of the proposed collaborative activities include: development of improved immunodiagnostic products; long-acting contraceptives (e.g. implants and injectables); approaches to male contraception, long-term safety of various contraceptive methods; reproductive epidemiology and surveillance; research on gonadal peptides and proteins; utilization of molecular biology in reproductive research; transgenic technology in medicine; and contraceptive drug delivery systems.

NICHD's extramural research program is supporting a number of population-related studies. A study funded by NICHD has provided evidence of declines in marital fertility among almost all social groups in four countries -- Indonesia, Malaysia, the Philippines and Thailand. An NICHD-supported analysis of survey data from 30 countries in Africa, Latin America, and Asia is examining two important components of fertility decline. One component is the reduction of desired family size, resulting from socioeconomic development, and the other is the reduction in unwanted births resulting from improved access to family planning.

Under a reimbursable services agreement with the Agency for International Development, the Centers for Disease Control continued to provide logistics assistance, perform contraceptive requirements analyses, conduct program evaluations, evaluate and collect program data, provide information and data to AID-assisted countries, and assist in the implementation of management support systems. During 1989, assistance was provided to 33 countries, including thirteen in Latin America, fourteen in Africa, two in Asia, and three in the Near East. Major program effort went into programs with Brazil, Ecuador, Haiti, Jamaica, and Swaziland. For example, in Brazil, CDC provided technical assistance in the survey design and data management for Young Adult Reproductive Health Surveys (YARHS) in three cities. Consultation was provided for survey design, field implementation and data analysis for the YARHS and for Vasectomy Attitude and Knowledge surveys in two cities.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

FAMILY PLANNING AND POPULATION RESEARCH

The National Institute of Child Health and Human Development (NICHD) has the primary responsibility for the research programs in the population sciences of the Department of Health and Human Services. Section 448 of Title IV of the Public Health Service Act as amended by P.L. 99-158 authorizes the Institute to conduct and support "research, training, health information dissemination, and other programs with respect to maternal health, child health, mental retardation, human growth and development, including prenatal development, population research, and special health problems and requirements of mothers and children." Section 1004 of Title X of the Public Health Act, as extended, authorizes the Department of Health and Human Services to award grants and contracts for "research in the biomedical, contraceptive development, behavioral, and program implementation fields related to family planning and population."

NICHD's Center for Population Research (CPR) is responsible for the primary Federal extramural program in population research. Support is provided through grants and contracts for:

- Fundamental biomedical research in the reproductive sciences relevant to the problems of human fertility and infertility.

- Development of safe and effective methods for fertility regulation.

- Evaluation of the benefits and risks of current contraceptive methods.

- Demographic and behavioral sciences research on the causes and consequences of population structure and change.

The support of population research and research training includes programs for institutional and population research manpower development. In addition, the Center encourages the dissemination of research information in the population sciences and promotes international cooperation in this area.

Reproductive Sciences

The program in the reproductive sciences--reproductive medicine, endocrinology, biology, genetics and immunology, and the developmental biology of reproduction--supports research to advance our knowledge of reproduction, which will expand our understanding of fertility-regulating mechanisms and provide new

approaches for alleviating or curing infertility, reproductive diseases, and disorders.

Dr. Steven S. Witkin, an NICHD grantee at Cornell University Medical College in New York City, New York, has investigated the possible relationship between the presence of sperm antibodies and either diminished conceptions or increased miscarriages in 109 infertile couples. Each couple was characterized with regard to pregnancy outcome over an 18-month period through the use of an assay to detect antibodies to the sperm on the surface of ejaculated sperm or in the woman's serum. Dr. Witkin found that antibodies to the sperm were present in the sera of 38.2 percent of the women who did not conceive and in 43.8 percent of the women who miscarried. In contrast, he only found the antibodies in 11.8 percent of the women with successful pregnancies. These results suggest that the presence of antibodies to sperm in female sera corresponds to a lowered probability of attaining a successful pregnancy due to an increased incidence of conception failures or early (first trimester) miscarriages.

Contraceptive Development

The contraceptive development program supports clinical trials and laboratory studies aimed at developing and improving fertility regulation methods for both men and women that are safe, effective, reversible, and acceptable to various population groups. Research goals include the development of new drugs and devices to regulate fertility in both sexes, improved methods of drug delivery, and better barrier methods of contraception.

Dr. Gerald S. Bernstein, an NICHD contractor at the Los Angeles Regional Family Planning Council in California, is completing the Phase II clinical study of the polyvinyl sponge containing benzalkonium chloride as the spermicide. In terms of contraceptive efficacy, the sponge has a failure rate approximately the same as the cervical cap and the diaphragm. Dr. Bernstein's preliminary analysis indicated a failure rate of 9.7 percent at six months of use and 17 percent at twelve months. Separation of the overall failure rate into its method and user failure components revealed a significant difference between sponge and cervical cap or diaphragm users. Over half of the matched sponge pregnancy rate was attributable to method failure. With the cervical cap or diaphragm pregnancy rate, only one-third was due to method failure. Conversely, user failure rates were lower for the sponge than for the cervical cap or diaphragm. These data support the concept that while both the cap and the diaphragm may be more effective than the sponge when used consistently, the ease of sponge insertion makes it more attractive to the contraceptive user.

Contraceptive Evaluation

The contraceptive evaluation program designs and supports clinical, epidemiological, and basic science studies to elucidate the safety and efficacy of fertility regulation and of all gynecological treatments and surgical procedures. A major emphasis of the program is to demonstrate the degree to which barrier contraceptives reduce the risk of gonorrhea, chlamydia and viral infections, including herpes and AIDS.

Dr. Andreas S. Stergachis, an NICHD contractor at Group Health Cooperative of Puget Sound (GHC) in Seattle, Washington, has completed a retrospective cohort study of the sequelae of tubal sterilization. The cases included 8,560 women aged 20 to 49 who had a tubal sterilization at GHC between 1968 and 1983. These women were compared to nearly 26,000 non-sterilized women who were matched at a 4:1 ration on the basis of birth year and year of first enrollment in the GHC health plan. A second comparison group of 4,155 wives of sterilized men, identified by GHC automated enrollment files, was used to control for factors associated with a couple's decision to permanently and surgically terminate childbearing potential.

Dr. Stergachis found an overall elevation in the risk of having a hysterectomy following tubal sterilization (relative risk = 1.58), with the relative risk rising to 3.4 for women who were sterilized at ages 20 to 29. A plausible explanation for this risk in younger women is that when a woman has a uterine disease that might require a hysterectomy, the physician would probably attempt to preserve her reproductive capability, while a physician might decide in favor of the hysterectomy in a woman with a prior tubal sterilization. Additional findings show an elevation in dilation and curettage and menstrual disturbances, particularly in women sterilized in the 20 to 29 age group. Sterilized women had a higher risk of pelvic inflammatory disease and a significantly higher rate of hospital admissions than the two groups of non-sterilized women. There was no evidence of an increase in breast cancer, endometrial cancer, endometriosis, or cardiovascular or cerebrovascular disease. The death rate of the sterilized women also did not differ from that of either comparison cohort.

Demographic and Behavioral Sciences

The demographic and behavioral sciences program focuses on the size, rate of growth, and composition of our Nation's most valuable asset, its population. Specific research projects are concerned with the growth and distribution of our population, and their relation to individual and societal welfare. The program's strategy concentrates on the questions of basic scientific concern and current societal importance.

In order to examine the interrelationships between women's employment, fertility, and child care, Dr. Karen O. Mason, an NICHD grantee at the University of Michigan in Ann Arbor, has studied approximately 1,400 mothers of preschool children residing in a metropolitan area. Nearly one-fifth of the sample of women who were out of the labor force or currently employed reported that they would either work, look for work, or work more hours if satisfactory child care were available at a reasonable cost. Twenty-six percent of the sample reported being constrained in their employment at some time due to child care problems, with the constraint being greatest among poor and minority women. Among women who said that their employment was currently constrained by child care problems, more than three-quarters indicated that they would find care by non-relatives satisfactory, and approximately 85 percent said that they would be willing to pay for this care. Dr. Mason also found that the woman who was paid a small hourly fee for child care relative to her income and wages, who has used child care for a large number of hours, and who perceives family day care homes to be available in her neighborhood has a higher probability of planning to work than do her counterparts facing different child care conditions. In contrast to constraints on women's employment, reported constraints of child care on women's fertility were relatively rare. Only about 10 percent of the sample of mothers indicated that child care problems had influenced either the spacing or numbers of births they had.

Future Directions of Family Planning and Population Research

Reproductive Sciences

Research in reproductive medicine will be aimed at the solution of problems of human infertility and reproductive disorders. Specific research areas may include diagnosis, mechanisms, treatment, and prevention of infertility, endometriosis, polycystic ovarian syndrome, and reproductive consequences of infections, including sexually transmitted diseases. Reproductive genetics and immunology studies will focus on the genetic basis of fertility and reproductive disorders, immunologic infertility, and the potential of immunocontraception. Reproductive endocrinology research will emphasize neuroendocrinology, pituitary, gonad, and genital tract factors; hormone action mechanism; and blastocyst (the fertilized egg at an early stage of division) implantation. Studies concerning the developmental biology of reproduction will involve the use of the most advanced biophysical and biochemical techniques of cell biology and cell physiology on oogenesis, fertilization, and preimplantation embryos of animals to study the more readily visible results of gene activity. Reproductive biology studies will include continued active exploration of the regulatory and modulatory roles of the various growth factors involved in reproductive processes.

Contraceptive Development

Clinical trials of new chemical copies (analogs) of luteinizing hormone-releasing hormone (LHRH)--a hormone that is produced in the brain and regulates reproductive processes--will be continued to ascertain the potential of these drugs for regulating fertility in men. Clinical studies will be initiated with new long-acting implants and injectables to ascertain their suitability as contraceptives. Clinical studies with new transdermal patches will be continued and research on other new patches will be solicited. With regard to barrier methods of contraception, the new disposable diaphragms and new spermicidal formulations will be evaluated, research on the development of new spermicides will be supported, and studies of new condoms for both the male and the female, involving new condom materials and designs, will be initiated. In the area of drug development, the synthesis and testing of LHRH analogs will be continued, the synthesis of male antifertility drugs will be expanded, and the screening of compounds for antifertility activity will be continued.

Contraceptive Evaluation

The evaluation of steroid hormone contraceptives will include continued investigation into the association between reproductive system cancer and long-term exposure to currently marketed contraceptive steroids, particularly in young women with additional cancer risk factors. Other reported benefits of contraceptive steroids, including the putative protective effect vis-a-vis rheumatoid arthritis, systemic lupus erythematosus, genitourinary diseases and toxic shock syndrome will continue to be evaluated. The monitoring of current oral contraceptive users for short-term side effects according to various pill formulations, such as the role of the pill in ameliorating or worsening premenstrual syndrome, will be supported. Research will be directed at understanding the relative safety and quantifying the failure rates of the established and newly emerging procedures for female sterilization, and ascertaining the long-term health effects of female sterilization. Surveillance of vital statistics will be used to quantify the findings that men who are vasectomized have a longer life expectancy. Clinical studies will be supported to compare the efficiency of various methods for the reversal of male and female sterilization procedures. The use-effectiveness of various barrier methods, including the new contraceptive sponge, will continue to be evaluated. Studies will be supported to ascertain and quantify the reduction in the risk of bacterial and viral sexually transmitted diseases (STD's) and pelvic inflammatory disease among women who use barrier methods of contraception. *In vitro* studies will be aimed at determining the maximally inhibitory spermicides against viral STD pathogens, including hepatitis and the human immunodeficiency virus.

Demographic and Behavioral Sciences

The problems associated with adolescent pregnancy and childbearing will be examined further in a major, national study of adolescents, which will bring together information about the teen, the peer group, the school and community context, and the parent and family in order to increase our understanding of adolescent behavior in this area. Research will continue to be supported on fertility trends and their relation to other demographic, social, and economic processes in the United States, such as the relationship between major changes in Americans' marital behavior, fertility behavior, and family experiences of children. The National Surveys of Family Growth and the National Longitudinal Survey - Youth Cohort, both partially supported by NICHD, provide an important data resource for analyzing fertility trends. In addition, research will proceed on the use of condoms to prevent transmission of AIDS, and on the relationships between STD's and fertility-related behavior. Studies will be supported to examine attitudes and behaviors about the desirability of bearing children biologically related to both parents, with particular relevance to the new technologies for infertility treatment, and about the costs of treating infertility. Research on intergenerational family relationships will continue to be funded on such topics as the effects of family disruptions on child socialization, the effect of parental employment on child development, and intergenerational transmission of attitudes and values. Studies concerning child care and fertility will examine the role of cost and availability of child care on the employment-fertility relationship. Research will continue to be supported dealing with migration, in order to understand better this most dynamic force shaping the population structure of American communities. Studies in the areas of infant mortality, low birth weight, and child health, including evaluations of the racial and ethnic differentials in low birth weight, will also continue to be funded.

FOOD AND DRUG ADMINISTRATION

FAMILY PLANNING

The Food and Drug Administration (FDA), authorized by the Food, Drug and Cosmetic Act of 1938 as amended, approves contraceptative drugs and devices for safety and effectiveness before they are marketed and maintains surveillance over them after they are marketed.

FDA involvement in population research and family planning services is directed toward:

Using its regulatory responsibility to assure the safety and effectiveness of contraceptive drugs and devices.

Sponsoring and/or monitoring the progress of research necessary to carry out the Agency's regulatory responsibilities relating to contraceptive safety and efficacy.

Maintaining a reporting system which serves as a clearinghouse for information concerning adverse reactions associated with contraceptives.

Providing expert advice to the pharmaceutical industry and the academic community in the conduct of studies to obtain data on the safety and efficacy of contraceptive drugs.

Soliciting the views of consumers and other interested parties on proposed public health policies and programs.

The first oral contraceptives (OC) were approved by FDA for general use in 1959. Because of growing concern over side effects to these drugs, FDA established the Advisory Committee for Obstetrics and Gynecology and in 1966 and 1969, the Committee published detailed reports on OCs.

This Committee, rechartered in 1977 as the Fertility and Maternal Health Drugs Advisory Committee (FMHDAC), participates in revising contraceptive labeling and in updating guidelines for clinical investigations of contraceptive drugs. The FDA Center for Devices and Radiological Health also has an advisory committee called the Obstetric and Gynecological Device Panel which has parallel functions, with oversight of contraceptive devices.

The Investigational Device Exemption (IDE) regulation became effective in 1981, and allowed sponsors with approved protocols the freedom to test the safety and efficacy of investigational devices on human subjects. Currently, two different IDEs are active with protocols approved to study the safety and effectiveness of cervical caps for contraceptive proposes. One model of the cervical cap was approved for marketing in 1988. The studies are closely monitored by the bioresearch monitoring program and the sponsor's required annual reports are thoroughly reviewed.

The FDA continues to assess the risk to fetal development from exposure to ionizing and non-ionizing radiation. The agency promotes consumer and professional education programs to encourage prudent use of diagnostic radiation examinations of pregnant women. Specific activities include:

Publication of recommendations to minimize diagnostic nuclear medicine exposure to the embryo, fetus, and Infant. A pamphlet, "X-Rays, Pregnancy, and You," was published which discusses the special considerations necessary to protect the developing fetus from adverse effects of medical radiation. This pamphlet is available in both English and Spanish.

A poster was prepared and distributed for display in physicians offices, clinics, and radiology departments to remind pregnant women to inform the doctor if they are or think they may be pregnant before obtaining an x-ray. This poster is available in both English and Spanish.

In response to growing interest and concerns, FDA examined video display terminals to determine if a radiation hazard to pregnant women existed. No radiation hazard was identified. FDA will continue to monitor these devices through a program of testing and surveillance.

In cooperation with professional organizations, FDA has continued an aggressive effort to determine the effects of ultrasound on the developing fetus.

FDA's Center for Devices and Radiological Health is working with the American Institute of Ultrasound in Medicine to develop educational materials directed to health professionals using fetal Doppler Ultrasound. The educational information will contain instructions on how to know and control acoustic output of their equipment during diagnostic procedures.

FDA's Epidemiology Branch conducts comparative analyses of birth defect data from both exposure cohort and defect registry studies, as well as drug experience case reports and other sources. For these analyses the possible association with birth defects of spermicides, oral contraceptives, and other fertility-related drugs is being constantly monitored.

Concerning intrauterine devices (IUDs), the FDA authority, prior to passage of the 1976 Medical Device Amendments, was limited to the misbranding or adulteration of non-drug intrauterine devices. FDA maintained surveillance over such marketed devices to ensure their safety and efficacy within its limited authority. As a result of the Medical Device Amendments of 1976, however, those IUDs which are not classified as drugs were placed under the control of the FDA Center for Devices and Radiological Health, and they are now subject to review for safety and efficacy.

To implement the 1976 Amendments, the FDA convened advisory panels to assist in classifying medical devices into three regulatory classes: Class I, General Controls; Class II, Standards; and Class III, Premarket Approval. Final regulations were published in 1980 classifying the following devices into the Premarket Approval category: IUDs, tubal occlusion devices, and hysteroscopic devices for female sterilization. Classified into the Standards category were: abortion devices, condoms, laparoscopic and culdoscopic devices for female sterilization, and diaphrams. FDA has classified fertility prediction devices into Class I (General Controls). These devices use basal body temperature and cervical mucus as a means to determine ovulation.

FDA approves new types of non-drug IUDs, new types of tubal occlusion devices and hysteroscopic devices for female sterilization for safety and effectiveness before they are marketed, and maintains surveillance over such devices after they are marketed. Devices that were already on the market prior to the passage of the Medical Device Amendments were allowed to remain on the market without submitting safety and effectiveness data until they were classified. For Class III devices, FDA must allow at least a 30-month grace period before initiating a procedure to call for the submission of safety and effectiveness data.

The Agency published a proposal to call for such submissions for non-drug IUDs in 1985. Two preamendments device IUDs have been withdrawn voluntarily from the market; the Safe-T-Coil in 1982 and the Lippes Loop in 1985. In 1986, Searle stopped the sale of its Copper-7 and Copper-T IUDs in the U.S. because of the company's concern for liability suits. One drug IUD, the progestasert, is still available and the copper IUD called T380A, was approved in 1984 and marketed in 1988. No non-drug IUDs are currently being marketed.

In October, 1987, FDA required the submission of safety and effectiveness data for tubal occlusion devices that are attached to the outside of the fallopian tubes (bands or clips). Since then FDA has received data for two of these devices and the Obstetrics and Gynecology Devices Panel has recommended that FDA conditionally approve both of them.

FOOD AND DRUG ADMINISTRATION

ACQUIRED IMMUNE DEFICIENCY SYNDROME

The conquest of AIDS has been identified by former President Reagan and President Bush as the nation's number one public health priority. The disease has reached epidemic proportions. Since it was first reported in 1981, over 100,000 persons in the United States have contracted AIDS, and more than half of these persons have died.

As the largest consumer protection agency of the Federal Government, FDA plays a major role in the Federal Government's response to the AIDS epidemic. FDA is responsible for assuring the safety and effectiveness of drugs, biologics, and medical devices and has responsibility for safeguarding the nation's blood supply. Clinical testing of AIDS therapies must be approved by FDA, and it is FDA's responsibility to determine whether those AIDS therapies are safe and effective for marketing in the U.S. FDA is exerting tremendous effort to expedite the development, review, and approval of promising therapies and, where appropriate, facilitate expanded access to promising investigational therapies to persons for whom no alternative therapies are available.

Research Activities

A strong program of scientific research is essential to maintain the quality and timeliness of FDA's review of AIDS products. Up-to-date expertise leads to authoritative product evaluation. Expertise in such areas as pharmacokinetics can aid manufacturers in designing trials that can streamline product approval. To enhance FDA's regulatory ability, a research program in cytokine biology has been established within FDA to study the basic immunologic defects associated with AIDS and to discover means to ameliorate these defects.

FDA is continuing its collaborative studies with the National Institute of Allergy and Infectious Diseases (NIAID) and the National Cancer Institute (NCI) in characterizing the immune responses, monitoring viral infection, and studying antiviral and immunotherapeutic drugs in AIDS patients. In addition, FDA has established collaborative efforts with other agencies in the accomplishment of these and other goals related to the treatment and prevention of AIDS and HIV infection.

Included in the research FDA conducts are studies on: (a) the adequacy of the processes used to prepare anti-hemophiliac factor (Factor VIII) and immunoglobulin in the inactivation of HIV; (b) the effects of antiviral compounds on replication of HIV; (c) the molecular biology of HIV; (d) primates to develop an animal model for AIDS; (e) the epidemiology and immunology of HIV infections as they relate to the safety and effectiveness of regulated products; (f) the significance of HIV infections with respect to safety of

biologic products; and (g) the etiology and pathogenesis of Kaposi's Sarcoma. Also, FDA licenses and monitors the HIV antibody test kits, and evaluates the safety of blood products. FDA is, in addition, funding studies to determine the safety and efficacy of AIDS vaccines, as well as the efficacy of blood donor criteria, and the testing for HIV antibodies and antigen in blood donors.

In order to focus attention on issues concerning blood screening and the safety of injected blood products, FDA has created a new laboratory of retrovirology. Among other things, the laboratory is engaged in research on detection of HIV infection by culture, gene amplification, and inactivation of virus in the manufacture of blood products. In addition, FDA has created a new Division of Cytokine Biology in response to the growth in recombinant products dealing with AIDS and AIDS-related diseases. FDA has also completed the construction of special laboratories to permit safe use of live HIV in some experiments.

New Drug Evaluation

It is FDA's responsibility to approve safe and effective drugs used in the care and treatment of AIDS patients. Special emphasis is being placed on producing the most timely and efficient premarketing review possible of drug products which offer promise for diagnosing, treating, or preventing AIDS and AIDS-related diseases.

FDA's strong commitment was demonstrated initially by the timely and thorough premarket review of the drug Retrovir, (Zidovudine, formerly known as AZT), the first drug approved for use in AIDS in March 1987. Retrovir was the first drug to go completely through the 1-AA designation process which was created in June 1986 as an extension of the existing classification system for review of New Drug Applications (NDAs). This designation was established to assure that all potential AIDS therapies would receive the highest priority in the drug review process. The expedited drug approval process has also resulted in the licensure of human interferon Alpha 2 for the treatment of AIDs-related Kaposi's Sarcoma, aerosol pentamidine for prevention of pneumocystis pneumonia, and ganciclovir for use in treating viral retinal infections among persons with AIDS.

As of November 1, 1989, FDA has received over 300 Investigational New Drug Applications (INDs) for approval to test new AIDS drugs, biologics, and vaccines in humans. Over 250 INDs remain active including 56 antiviral drug INDs, 63 immunomodulator INDs, nine vaccines, five anti-neoplastics, 56 INDs for drugs for opportunistic infections, 47 diagnostics, and 20 hematologic-related factors. The number of applications for new investigational AIDS therapies reviewed by FDA has averaged about six per month in 1989.

Six Treatment INDs have been approved since the Treatment IND regulations became effective in June 1987. Four remain active,

the other two, for aerosol pentamidine and ganciclovir, terminated upon product approval in June 1989.

In addition, ddI, a new antiretroviral drug, has been made more widely available both under a Treatment IND and through an open safety protocol in parallel with the phase II controlled clinical trials, a new approach to combining the drug development process with wider treatment availability.

FDA's other special initiatives in the area of new investigational AIDS therapies include improvements in management such as: plans for development of an on-line computerized tracking system for all AIDS review activities, including INDs, NDAs, PMAs (Pre Marketing Applications), and other drug/biologic applications; development of the FDA component of the National AIDS Clinical Trials Information Service, a database providing public access to information about AIDS-related clinical trials; creation of the Division of Antiviral Drug Products; creation of the AIDS Coordination Staff to promote intra-and inter-agency cooperation on crosscutting issues; establishment of a special team approach to provide selected pharmacokinetic data and guidance as needed to sponsors; and a series of workshops with the Institute of Medicine and others on clinical trial design for premarket evaluation of AIDS-related products. In addition, FDA is working closely with the National AIDS Program Office, the National Institutes of Health, other governmental and private organizations and concerned individuals to develop a "parallel track" policy whereby promising new investigational therapies can be made available to persons with AIDS and HIV infection who cannot participate in controlled clinical trials.

HIV Detection

Progress continues on the development of satisfactory test methodologies for HIV antibody detection. To date, there are ten licensed manufacturers of HIV antibody test kits including ELISA screening tests, one particle-agglutination screening test, and one Western Blot test. Currently, there are more than 15 pending applications for new kits or amendments for refining existing ones. In August 1989, FDA licensed the first diagnostic kit to detect the presence of HIV by directly detecting the proteins, or antigens, of the virus. This new HIV-1 antigen test is approved to help physicians diagnose and follow the medical status of HIV-infected persons. It is not intended for use in screening blood or plasma donations.

Among the new product applications are several forms of testing which need to be validated for clinical use. These include:

1. Additional tests to detect circulating viral antigen during various phases of HIV infection with potential clinical applications.

2. Antibody screening test using viral antigens produced by gene cloning or peptide synthesis. Such recombinant peptide-based tests may offer improvements in the sensitivity and specificity of antibody detection and may also facilitate the development of rapid and inexpensive tests for widespread use. In addition, the use of recombinant peptides may greatly reduce the risks posed to laboratory workers involved in the manufacture of antibody test kits.

3. Several new product applications have been received for Western Blot and immunofluorescence tests.

4. Screening assays designed to detect antibodies to other retroviruses (i.e., HIV-2). Regulation of these products has raised issues similar to those handled by FDA in relation to the regulation of the first HIV screening tests such as the development of reference reagents and criteria for measuring sensitivity and specificity.

5. Test kit manufacturers have submitted amendments for the use of dried blood spots as a sample source for HIV antibody testing. Such procedures would facilitate public screening. Review of FDA policy concerning such test kits is under way.

In November 1989, FDA published in the Federal Register a notice to all manufacturers of in vitro tests for HIV antibody, and other interested parties "points to consider" in the manufacture and clinical evaluation of such test kits. This notice addresses the non-regulatory questions most frequently asked concerning the evaluation and approval of HIV antibody test kits and is intended to facilitate communication between the Agency and individuals interested in making applications to FDA.

HIV antibody testing, continuing in all blood banks, donor centers and plasmapheresis centers, has been augmented by the licensed Western Blot test which serves as the basis for reentry of blood donors tentatively deferred because of nonrepeatable, false-positive results from initial screening. Use of the Western Blot has remarkably upgraded the specificity of information derived from donor screening. Also, use of this test in a reentry algorithm has permitted approximately 80 percent of deferred donors to be reinstated without compromising blood safety.

Universal HIV testing of donated blood and blood products has reduced the rate of confirmed positive antibody tests in donors. This change may be due to several factors which include permanent exclusion from the donor pool of individuals with detectable

antibodies as well as successful implementation of education and self deferral programs in blood and plasma centers. A reduction in the rate of HIV antibody positive donors implies increased safety of blood and blood products available for use in the U.S.

FDA revised the package insert labeling of HIV antibody test kits to permit a claim for clinical diagnostic use. This has made testing more widely available for purposes other than blood screening. Consideration is also being given to developing testing programs, home sample collection, mail-order testing, and notification. While such programs would offer the public wide access to HIV tests at a high level of confidentiality, significant problems are posed for effective regulation of the testing and assurance of adequate counseling following a positive test result. FDA has published a proposed rule which would restrict such mail-order testing to collections obtained in a comprehensive health care facility, has held a public hearing on the proposed rule, and is reviewing public comment now.

FDA recently approved licensure of antibody screening tests for another human retrovirus, HTLV-1, which is not associated with AIDS, but which causes a rare leukemia and a neurological disorder. The FDA has recommended screening of blood intended for transfusion since studies in the U.S. have confirmed a significant prevalence of infection by this virus in blood donors, and it is known that certain blood components can transmit the virus to recipients. FDA is continuing its involvement in surveillance testing of U.S. populations to identify the possible introduction of a new class of AIDS-causing retroviruses, called HIV-2, which has already been detected in some countries in Western Europe.

Progress continues in the development of improved methods of virus inactivation in antihemophilic factor preparations. In particular, liquid pasteurization in the presence of protein stabilizers and treatment with detergents and organic solvents seem to offer significant benefits. The use of monoclonal antibody columns offers an additional method of improving virus clearance while also increasing the specific activity of the materials. Products have been licensed which use these technologies, and an effort is ongoing to upgrade the industry standards for acceptable inactivation of virus in these products.

In addition to assisting in the organization of workshops dealing with the proper use and interpretation of antibody tests, FDA also sponsored a large scale study on the effectiveness of HIV antigen testing as a screen for donated blood or plasma. The study involved over 500,000 donors and indicated no improved safety by the addition of the antigen test kit to the current screening procedures for blood and blood products. Similar efforts have been undertaken to define the role of HTLV-1 antibody testing in blood bank screening. FDA has developed contracts for the management of large serum repositories which can be used to validate the sensitivity of commercial tests for HIV and HTLV-1 antibodies. FDA supports the World Health Organization in its efforts to develop

international guidelines for HIV test evaluation and standardization particularly in the area of interpretation of Western Blot and other tests used to confirm antibody screening tests.

HIV Transmission - Blood

As noted previously, protection of the nation's blood supply is an ongoing FDA regulatory responsibility which has become vital in the context of the AIDS epidemic. Although the risk of acquiring human immunodeficiency virus by transfusion of blood has almost been eliminated with blood and donor screening efforts, FDA expanded its inspections of blood collection facilities to ensure the presence of effective quality controls and to ensure compliance with requirements for HIV testing. In 1988, FDA increased its inspections of all such FDA regulated facilities in the U.S. from biannually to annually. Although these inspections revealed slight deviations in procedures from FDA regulations, no confirmed HIV antibody positive (HIV contaminated) units had been transfused. Regardless of this, FDA plans to continue this expanded effort in order to ensure that the safety of the blood supply is sustained and continues to promote the use of autologous, instead of homologous, blood for elective procedures that may require transfusion.

Due to a number of reported cases of HIV transmission, much attention has been given recently to the problems of insuring the safety of health workers and laboratory workers involved in the handling and processing of blood. In particular, consideration is being given to the adoption of universal blood precautions and to the strict adherence to published biosafety guidelines for sample handling and processing. FDA continues to work with the Centers for Disease Control and other agencies in efforts to define improved ways to reduce the risk of exposure to HIV through the handling of blood and blood products.

HIV Transmission - Medical Devices

In its ongoing responsibility to assure the safety and effectiveness of medical devices, FDA has launched a program that concentrates on preventing the transmission of AIDS and AIDS-related diseases through such barrier products as condoms and surgical gloves and commonly-used clinical devices such as dental drills. FDA is surveying the methods of disinfection of clinical devices to learn how sterilization procedures may be improved and is working with device manufacturers to improve device design in ways that minimize risk.

In the field, FDA is inspecting manufacturers and processors of both domestic and foreign-made condoms to ensure conformance with FDA's criteria for acceptability. Since implementation of this program, FDA has tested over 180,000 condoms from about 700 batches of condoms. Batches with more than four defects per 1000 condoms were not permitted to reach the U.S. market. These efforts are

leading to increased quality control by manufacturers. In 1988, FDA increased its surveillance of surgical and examination gloves, testing over 26,000 individual gloves on the market. Failure rates were found to be high, particularly in shipments of imported gloves, and FDA developed a more stringent and sensitive method to test glove integrity in order to improve the quality of medical gloves. In November 1989, FDA published a Federal Register Notice to establish a sampling and testing program for the examination of surgical gloves. In addition to these ongoing inspection efforts, FDA is continuing research into improvement of barrier effectiveness, as well as efforts to expedite the review of an increasing number of applications for approval of these products.

Vaccines

FDA has studied the immunology of AIDS and demonstrated that some proteins of HIV are targets for human immune responses and could be used in developing a vaccine against the virus. A rapid and sensitive microneutralization assay has been developed and is being used to evaluate the specificity of immune responses induced by candidate vaccines. Studies are continuing to develop information necessary for evaluation of vaccine safety and efficacy. FDA has begun developing potency tests for candidate AIDS vaccines. In addition, studies to characterize four cellular immune responses to HIV antigens are in progress. Cell-mediated responses may come to play an important role in vaccine-induced disease prevention.

FDA is defining issues that should be addressed prior to initiation of Phase I vaccine clinical trials and in anticipation of efficacy studies. FDA has frequent joint meetings with manufacturers of candidate vaccines. Manufacturers are encouraged to request such meetings as early and as frequently as needed. These meetings assure the exchange of information that will facilitate preclinical and clinical development and IND review. FDA continues its policy of reviewing AIDS-related IND applications for vaccines as quickly as possible. To date, nine IND applications for AIDS vaccine have been received, and several have been approved for Phase I clinical studies.

Extramural studies related to evaluation of the safety and efficacy of AIDS vaccines are being conducted worldwide. Collaborative studies with investigators in the U.S., Europe, the Caribbean, Africa, and South American have begun to look into immune responses to HIV infection. Information derived from these studies will be directly applicable to AIDS vaccine development.

Other Areas of Activity

The Agency is compiling a compendium of information on nutritional needs of persons with AIDS as part of an effort to improve the health quality of those affected by HIV.

A video on food safety, recently developed and released by FDA and the Centers for Disease Control and aimed at preventing transmission of foodborne illness among persons with AIDS and HIV infection, has been well received by the public.

FDA is also developing a brochure which provides the same food consumption and handling advice for persons with AIDS and will distribute it through the National AIDS Information Clearinghouse.

FDA has developed state contracts to establish AIDS Health Fraud Task Forces in 17 states, District of Columbia, and Puerto Rico. These task forces will include the FDA district AIDS coordinators, state AIDS coordinators, community-based organizations, health care professionals, state and local health agencies, state attorneys general offices, United States postal inspectors offices, and consumer groups. These task forces will ensure that information concerning AIDS fraud is distributed quickly and that necessary action to prevent AIDS health fraud can be taken.

FDA has developed a booklet to educate condom users regarding prevention of HIV and other sexually transmitted diseases. This brochure has been prepared with consultation and encouragement from 12 governmental components and 8 national health professional organizations. The Agency has also developed an educational project for patients and health professionals concerning renal dialysis and AIDS as well as a program in conjunction with other health agencies to educate dental professionals about AIDS and infection control.

FDA communicates with health professional organizations, community-based research groups, individual physicians, as well as selected international organizations and foreign regulatory authorities on such topics as Treatment INDs, investigational products, and newly marketed FDA-regulated products for the diagnosis, treatment and prevention of HIV infection, AIDS, and AIDS-related conditions.

In support of its interest in and commitment to community-based research, the Agency works with public and professional organizations to encourage useful and effective research studies to support AIDS-related product approval. FDA has sponsored workshops to provide community physicians and other community-based researchers with the information and technical assistance necessary to meet FDA requirements for conducting clinical trials. FDA staff have also participated in similar workshops sponsored by other agencies and private organizations. FDA is also working closely with the Community Clinical Research Program in the NIAID's AIDS Program to coordinate activities and provide assistance in training their contract grantees.

HEALTH RESOURCES AND SERVICES ADMINISTRATION

Bureau of Maternal and Child Health and Resources Development

FAMILY PLANNING

The Office of Maternal and Child Health of the Bureau of Maternal and Child Health and Resources Development is involved in the provision of family planning services through the support of individual States which have chosen to provide such services as part of the Maternal and Child Health (MCH) Block Grant. Prior to enactment of the Omnibus Budget Reconciliation Act of 1981, (P.L. 97-35), family planning services were among those supported through the MCH formula grants program to States. Since needs in the family planning area in ways which reflect the particular circumstances of each State.

Many States have combined Title X and Maternal and Child health activities into a coordinated health care focus. Among the States, the degree of financial support for family planning services from the MCH Services Block Grant caries a great deal. Information on this topic is not required in the Block Grant annual reports, and therefore data on this subject are not available. Federal Maternal and Child Health staff provide consultation and technical assistance concerning family planning programs as part of their general responsibilities to assist States in development of comprehensive maternal and child health care systems.

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HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Maternal and Child Health and Resources Development

MATERNAL AND CHILD HEALTH

The Maternal and Child Health (MCH) Services Block Grant program was initiated in Fiscal Year (FY) 1982. The program consolidated the following former categorical grant programs: MCH Grants to States; MCH Research and Training; SSI Disabled Children's program; and Crippled Children's Services; Genetic Diseases; Hemophilia; Sudden Infant Death Syndrome; Lead-based Paint; and Adolescent Pregnancy.

The MCH Block Grant program provides formula allocations to the States to enable the States to maintain and expand a broad range of health care services, including preventive, primary care, and rehabilitative services, to mothers and children. Up to 15 percent of total funds available have been allocated to research and training, genetic disease testing projects, hemophilia treatment centers, and other special projects of regional or national significance. In FY 1989, 440 such grants were supported.

In FY 1990, 85 percent of total funds will again be allocated to the states on a block basis and 15 percent will be available for special projects grants of regional and national significance. All 50 States, the District of Columbia and nine Insular Areas will receive and administer the MCH Block Grants. In addition, approximately 450 special projects will be supported with 15% set-aside funds.

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HEALTH RESOURCES AND SERVICES ADMINISTRATION

Bureau of Health Professions

Family Care

Training and educational activities supported by the Bureau through its grantees with respect to health issues affecting women fall within several reporting categories. Maternal and child health activities emphasize the enhancement of training in high risk pregnancies, dealing with adolescent pregnancies, and generally improving OB/Gyn curricula. Child/family abuse activities also focus on problems related to spousal abuse, and information has recently begun to be gathered for sexually transmitted disease components incorporated into the training of physician assistants. At least three Physician Assistant training programs incorporate women's health initiatives which particularly assist disadvantaged women. This training includes pre/post partum care and midwifery.

The Nurse Practitioner and Nurse Midwifery Program awarded $3,676,727 to 23 schools to develop similar programs. While the programs supported under both authorities have much in common, the Nurse Practitioner programs are more likely to stress health promotion and maintenance, rather than the more acute conditions that are characteristic of Advanced Nurse Education projects.

In FY 1989 the Nursing Special Project program awarded $369,010 for activities in family care. These projects included support for improvement of clinical nursing practice through the incorporation of health promotion and health maintenance concepts during all stages of the life cycle within the family.

The Advanced Nursing Education Program awarded $215,985 to 3 schools in Fiscal Year 1989 to support programs designed to educate nurses to work with family groups. This care is comprehensive and may follow the family or family member from health and the home, rehabilitation and, hopefully, back into the community.

Women's Health Initiatives

Under the section 786(a) Family Medicine Residency program, nine grantees indicated training initiatives in this area. Four of these grantees received a total of $159,719 for development and expansion of curriculum in high risk OB/Gyn and prevention and management of teenage and other high risk pregnancies. St. Joseph's Hospital received $83,500 of the total funds for the purpose of revamping their OB/Gyn curriculum. It is estimated that 95 residents among these grantees will benefit from this improved training.

Child/Family Abuse Activities

Nine General Internal Medicine and General Pediatrics Residency program grantees indicated activities in child/family abuse, and requested a total of $25,234 specifically for this purpose. The Boston City Hospital also indicated that their faculty development program includes a child/family abuse component.

Under section 786(a) Family Medicine training, one predoctoral program offers child abuse educational experiences, as does one residency training program. No specific funds were requested by these grantees for efforts in this area.

INDIAN HEALTH SERVICES

Family Planning

The Indian Health Service (IHS) provides comprehensive, informed family planning services to all American Indian and Alaska Native men and women who request such services. The goal of these activities is to assure that all American Indian and Alaska Native children are wanted, born to healthy mothers, and born well. A very important aspect of this effort is that appropriate technical information and services are presented in a culturally acceptable and effective way.

Specific activities for adolescent and pre-adolescent groups are developed and implemented to reduce unplanned and adolescent pregnancies. Effective educational activities and programs geared at enhancing the self-image and self-esteem of Indian and Native youth are integrated into the IHS health care delivery system.

Efforts to increase and coordinate existing services to infertile couples continue. Infertility services and adoption services in coordination with other agencies are provided with limited resources.

The IHS does not have a budget line item for family planning. These services are provided as part of the overall comprehensive health care service program of the IHS.

The Area Health Education Center program awarded a total of $106,543 to 7 of the 8 projects who are offering educational training in the area of child/family abuse. The largest award was made to the University of Medicine and Dentistry of New Jersey ($74,923) for its special initiative in this area. The projects indicated that 7,635 individuals would be impacted by these activities.

Finally, 4 Physician Assistant Training programs are offering training to an estimated 73 students in the area of child/family abuse. Only one grantee requested specific funds ($300) for their activities.

Adolescent Health Activities

The Division of Medicine awarded a total of $374,321 to 57 grantees specifically to support educational activities in adolescent medicine. These efforts are estimated to impact approximately 83,013 individuals.

Nine Family Medicine Residency grantees indicated that an estimated 208 residents would receive training in adolescent medicine, but specific funds for this experience were not requested. One Family Medicine Predoctoral Program grantee also offers an educational component in adolescent medicine, but did not indicate a specific amount of funds for this area. One Family Medicine Faculty Development grantee has included adolescent medicine in its program activities.

Under the General Internal Medicine/General Pediatrics Residency program 25 grantees indicated training activities in adolescent medicine. Six of these programs received total funds of $139,073 specifically for these activities which would impact approximately 300 residents. Three Faculty Development programs are focusing on adolescent medicine.

The Area Health Education Center program had 12 projects with adolescent health curricular activities. A total of $234,313 was awarded to these programs, with the largest award ($39,467) to the Medical College of Ohio AHEC program for their special initiative in this area. The AHEC programs indicated that their educational interventions would impact approximately 82,288 individuals, including students and populations in the areas served by the projects.

Five programs to train Physician Assistants under new Section 788(d) indicated that an educational component would be offered in adolescent medicine, which will benefit an estimated 215 trainees. One grantee indicated that $935 of their award was directed toward this activity.

One AIDS Education and Training Center Program project offers training on the impact of HIV/AIDS epidemic on the adolescent population.

CENTERS FOR DISEASE CONTROL
Center for Chronic Disease Prevention and Health Promotion
Population and Family Planning

The reproductive health activities of the Centers for Disease Control (CDC) are targeted at public health problems associated with pregnancy, infant health, and fertility control. These activities include epidemiologic studies and surveillance that measure the patterns and trends of reproductive health outcomes and identify ways of reducing health risks. The CDC is also involved with the development and transfer of survey, epidemiologic, and evaluation technology to State and local health department programs.

The CDC conducts epidemiologic studies of the medical consequences of fertility control methods. Currently, more than 40 million women in the United States have used oral contraceptives at some time in their lives. However, the long-term effects of oral contraceptive use are not completely known. The CDC, in collaboration with the National Institute of Child Health and Human Development (NICHD), conducted a large-scale epidemiologic study to answer questions relating to oral contraceptive use. This study focused on the association between oral contraceptive use and the risk of breast, endometrial, and ovarian cancers.

Results indicate that women who have used oral contraceptives are approximately half as likely to develop ovarian and endometrial cancer as women who have never used them. Results from the study also indicate that oral contraceptive use does not increase a woman's overall risk of breast cancer. This information has been reassuring in the midst of an ongoing controversy regarding breast cancer risk. Further analyses of the relationship between oral contraceptive use and breast cancer are ongoing.

The CDC has recently reevaluated the risk of pelvic inflammatory disease associated with use of the intrauterine device (IUD). Results from a reanalysis of a large epidemiologic study suggest that women at low risk for sexually transmitted diseases may have little additional risk of pelvic inflammatory disease from IUD use. This information has been useful for family planning providers to help advise potential IUD users.

Another major area of investigation related to the medical consequences of fertility control is the study of early and late sequelae of tubal sterilization. This multicenter prospective study is following 11,000 women undergoing sterilization and 1,000 nonsterilized women as controls for a period of 5 years. The follow-up experience of these women will help to characterize better the health consequences of female sterilization, which is now the most prevalent method of contraception among U.S. women. Preliminary data indicate that approximately 4 percent of women regret having undergone sterilization at 5 years after the procedure. Young age at sterilization is the most important pre-operatively identifiable determinant of the likelihood of regret. Approximately 2 per 1,000 study participants had undergone a sterilization reversal operation by 5 years after sterilization.

Epidemiologic analysis of the incidence and causes of pregnancy-related morbidity and mortality in the United States continues to be a major CDC activity. Analysis of ectopic pregnancy mortality data for 1970-86 showed that the risk of death from ectopic pregnancy declined for all women of all ages, all races, and in all regions. However, women of black and other minority races continue to be at significantly increased risk of death from ectopic pregnancy compared to white women. Based on previous studies, CDC estimates that a substantial proportion of pregnancy-related deaths is not included in the tabulations of maternal mortality rate due to misclassification. To improve pregnancy-related mortality reporting and to determine risk factors for maternal mortality, CDC, in cooperation with State health departments and the American College of Obstetricians and Gynecologists (ACOG), has recently completed a retrospective study of all maternal deaths that occurred in the United States during 1979-86. The CDC has also initiated prospective surveillance of pregnancy-related deaths beginning with deaths that occurred in 1987. In addition to these ongoing activities, CDC is working with South Dakota on their maternal mortality surveillance and review process and providing technical assistance to Kansas to complete analysis of maternal deaths over the past 100 years.

Since 1969, CDC has collaborated with State Health Departments to compile the only official national surveillance reports on the number and characteristics of women obtaining induced abortions. Final statistics for induced abortions occurring during 1984-1985 and preliminary statistics for induced abortions occurring during 1986-1987 were published in CDC's Morbidity and Mortality Weekly Report. When compared with similar measures obtained in 1980, the rates and ratios of induced abortion did not change significantly. Most women obtaining abortions continue to be younger than 25 years (59%), white (66%), unmarried (73%), and with one or no previous live births (76.4%). Most abortions were performed during the first trimester (i.e., at or before 12 weeks of gestation (89%), and by curettage (97%). States are now submitting data for abortions that occurred during 1988.

The CDC provides training to Epidemic Intelligence Service (EIS) officers of the United States Public Health Service. Selected individuals in the EIS Program, as well as other CDC career staff and international health professionals, are trained in an epidemiologic approach for evaluating family planning, maternal/child health, and population programs. EIS officers, career staff, public health advisors, or other trainees have been assigned to States to work in the area of family planning evaluation. Currently, a CDC epidemiologist is working with South Carolina on a postpartum survey that will be administered to women prior to discharge from the hospital. The survey will assist in determining the family planning needs of these women.

The CDC provided major technical and programmatic assistance in family planning and maternal/child health programs to a number of States (26), Federal agencies, and other organizations during FY 1989. A particularly significant area of assistance focused on clinic management activities using models and techniques originally developed and applied to family planning clinics. The Patient Flow Analysis (PFA) system, designed and developed by CDC, has been used extensively to improve the efficiency of family planning clinics. The system has been adapted for use with a microcomputer to enhance its transfer to State and local health departments. A generic version of this system has been developed, expanding its use to other types of outpatient clinics. The PFA technique has been tested by the Social Security Administration (SSA) for use in their client setting to improve services to clients in local SSA offices.

During late 1986, CDC embarked on a major clinic management project with the Florida Department of Health and Rehabilitative Services that resulted in the establishment of a central Clinic Management Unit at the State level. Two initial groups, totaling 25 counties, implemented PFA studies, analyzed results, requested computer simulations of proposed changes, and made operational changes to improve their clinics. The final phase of the Florida Clinic Management Project has been completed, with all counties now using the clinic management technology.

During early 1989, a new CDC Clinic Management Unit (CMU) was formed to provide a focus for this activity and improve responsiveness to the field. The unit was charged with the following operational objectives:

- Transfer technology to State and local health departments.
- Serve as a intervention implementation resource for CDC.
- Create a clinic management information resource.
- Transfer technology to public health agencies in other countries.

A major project modeled on the completed Florida project was started in Kentucky, and in 1990 two more similar projects will be started. In addition, assistance is being provided to the Coast Guard Medical Services, and the Division of Primary Care of Bureau of Health Care Delivery and Assistance (BHCDA).

The CDC also provides technical assistance on medical, epidemiologic, and research issues in support of the Title X Family Planning Program through a Memorandum of Agreement with the Office of Population Affairs (OPA). A key accomplishment in 1988 has been the development of a report intended to provide guidance to family planning providers concerning the appropriate scope and level of AIDS prevention activities. Other projects included provision of technical assistance to the OPA on development of the Program Instruction on AIDS Education, Counseling and Testing in Title X, which was distributed to Regional Health Administrators in 1988, and technical reviews of specific documents upon request.

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CENTERS FOR DISEASE CONTROL
National Center for Health Statistics
Family Planning Information

The major data activity of the National Center for Health Statistics (NCHS) in the area of family planning is the National Survey of Family Growth (NSFG). This survey is designed to provide national statistics on the fertility, family planning, and reproductive health of American women in the childbearing ages.

The first and second cycles of the survey were conducted in 1973 and 1976, respectively, and were based on samples of women 15-44 years of age; never married women were excluded. More than 100 NCHS reports and journal articles from Cycles I and II have been published, and public use data tapes for further scientific research have been released.

Interviews for Cycle III were taken in late 1982 and early 1983, and the sample included women 15-44 years of age in all marital status categories. A public use data tape from Cycle III, for scientific research, was released in 1984, and an overview of the principal findings has been published. As of December 1989, at least 63 reports and articles based on Cycle III have been published, including 5 advance data reports and 7 series reports. Series 23 reports have been published on Contraceptive Use; Services for Family Planning and Intertility; Fecundity, Infertility, and Reproductive Health; Married and Unmarried Couples, Sample Design and Methodology; and Health Aspects of Pregnancy and Childbirth. Journal articles have examined topics such as trends in contraceptive use, the effectiveness of contraceptive methods, adoption, infertility, pregnancy outcomes, and teenage sexual activity.

Work on Cycle IV is under way. The pretest was conducted in September and October 1986 and evaluated in November 1986 through January 1987. Interviewing for Cycle IV was conducted in January through August 1988 with 8,450 women 15-44 years of age interviewed. Processing and editing of the data are under way. A public-use computer tape and the first published findings from the survey are expected in January 1990.

Planning for a telephone reinterview of the women interviewed in 1988 has begun. Tentative plans are to interview a sample of women 17, 34, and 52 months after their initial (1988) interview. This telephone followup will permit more frequent and more timely updating of program-relevant statistics and show changes in individual behavior over time.

The NSFG provides data on a wide range of specific topics related to childbearing and reproductive health in the United States:

- Trends in premarital sexual activity and contraceptive use among teenagers.
- The characteristics of adoptive parents and of women who relinquish babies for adoption.
- Pregnancy outcomes, the planning status of pregnancies, and intended future births.
- Trends and group differences in sterilization, infertility, pregnancy loss, and breastfeeding.
- The contraceptive methods used by women and their partners and the use-effectiveness of those methods.
- Use of family planning and infertility services (both public and private).
- Knowledge and prevalance of AIDS and other sexually transmitted diseases such as chlamydia and genital herpes.
- Use of child care services and the work experience and occupation of mothers in relation to their childbearing.

Cycle V of the NSFG is scheduled for 1992 and will be based on a sample of women initially interviewed in the National Health Interview Survey (NHIS) in 1991. This opens innovative opportunities for obtaining prospective information on issues concerning reproductive health from the two surveys for the same sample of women. The final reinterview of women initially interviewed in Cycle IV (1988) will also be coordinated with Cycle V (1992) interviewing.

The survey provides important baseline and evaluation data for a variety of health programs. The value of the data from the survey is reflected in the funding support given by such agencies as the National Institute for Child Health and Human Development and the Office of Population Affairs. The results of Cycle III and of Cycle IV will provide fundamental data for monitoring the specific decade objectives for family planning in the Department's program for "Promoting Health and Preventing Disease."

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CENTERS FOR DISEASE CONTROL
International Health Activities

Under a reimbursable services agreement with the Agency for International Development, the Centers for Disease Control continued to provide logistics assistance, perform contraceptive requirements analyses, conduct program evaluations, evaluate and collect program data, provide information and data to Agency for International Development (AID)-assisted countries, and assist in the implementation of management support systems. During FY 1989, assistance was provided to 33 countries, including 13 in Latin America, 14 in Africa, 2 in Asia, and 3 in the Near East. Major program effort went into programs with Brazil, Ecuador, Haiti, Jamaica, and Swaziland.

III

THE OFFICE OF HUMAN DEVELOPMENT SERVICES

The Office of Human Development Services' (OHDS) primary mission is to administer social service programs that address the needs of target populations which include children, youth, families, the developmentally disabled, Native Americans and the elderly. HDS provides technical and financial assistance to States and communities for programs that protect vulnerable children and adults, help families stay together and enable low-income and handicapped people to become self-sufficient.

Social Services Block Grant

The Office of Policy, Planning and Legislation, staff office to the Assistant Secretary of OHDS, is responsible for the administration of the social services block grant program (SSBG), the major source of Federal funding for social service programs in the States. Public Law 97-35, enacted August 13, 1981 amended title XX of the Social Security Act to establish the SSBG program under which formula grants are made directly to the 50 States, the District of Columbia, and the eligible jurisdictions (Puerto Rico, Guam, Virgin Islands, American Samoa and the Commonwealth of the Northern Mariana Islands) for use in funding a variety of social services best suited to the needs of individuals and families residing within each State.

In fiscal year 1989 a total of $2.7 billion was allotted to the States and the jurisdictions under the SSBG. The Federal government makes allotments under a formula based on each States's population. Each State has the flexibility to determine what services to provide, who is eligible to receive services, and how to distribute funds among the various services offered within the State. Thus, under the SSBG, family planning services are provided at a State's option.

Under the SSBG, each State must submit a pre-expenditure report to the Secretary on the intended use of the funds. The statute requires that the report include information about the types of activities to be funded and the characteristics of the individuals to be served. An analysis of the fiscal year 1989 pre-expenditure reports shows that 29 of the 56 States and eligible jurisdictions provided family planning services under their social services block grant programs. Family planning services are administered by the States and may include: information on available resources, personal counseling, and referral for medical care and follow-up. OHDS does not have the specific eligibility and expenditure data on State family planning activities as the SSBG program does not include detailed reporting requirements for such services.

IV

HEALTH CARE FINANCING ADMINISTRATION (HCFA)

Family Planning

Title XIX provisions require States to provide medical assistance to the categorically needy. In general, these are individuals who meet the financial eligibility requirements of a related cash assistance program - Aid to Families with Dependent Children and Supplemental Security Income. If they choose to, States may also provide medical assistance to a number of optional groups including the medically needy - individuals whose income exceeds the categorically needy but is not enough to pay for their medical care.

Family planning services were originally included in the Medicaid program as a State option. However, P.L. 92-603, enacted in October 1972, made coverage of family planning services for the categorically needy mandatory upon the States. This law also increased the rate of Federal financial participation for family planning services and associated administrative costs for both categorically and medically needy to 90 percent (rather than the lower percentage authorized for most other Medicaid services).

Current law requires States to furnish family planning services and supplies, directly or under arrangements with others, to Medicaid recipients of child bearing age (including minors who can be considered to be sexually active) who desire such services and supplies. The scope of family planning services varies among the States. Many States offer a comprehensive range of services to eligible individuals, while others limit family planning services to those furnished by or under the direction of a physician.

Title XIX regulations do not define family planning services with the exception of sterilization, which is subject to strict Federal requirements on obtaining the informed voluntary consent of the individual who must be at least 21 years old.

HCFA has determined that $224.9 million was expended by the States and the Federal government for family planning services in FY 1988. Approximately $67.5 million was spent for sterilization and an estimated $157.4 million for all other family planning services (expenditures and recipients under Medicaid for fiscal years 1988 through 1995 are reflected in Tables HCFA-1 and HCFA-2).

TABLE HCFA-1

ESTIMATED FEDERAL, STATE, AND LOCAL
FAMILY PLANNING EXPENDITURES UNDER TITLE XIX, FY 1988 - FY 1995

(IN MILLIONS OF DOLLARS)

	FY 88	FY 89	FY 90	FY 91	FY 92	FY 93	FY 94	FY 95
Total Expenditures	$224.9	$244.7	$273.6	$291.7	$308.7	$325.4	$341.2	$356.3
Sterilization Services	67.5	73.4	82.1	87.5	92.6	97.6	102.4	106.9
Other Family Planning Services	157.4	171.3	191.5	204.2	216.1	227.8	238.9	249.4

TABLE HCFA-2

ESTIMATED FEDERAL, STATE, AND LOCAL
FAMILY PLANNING EXPENDITURES UNDER TITLE XIX, FY 1988 - FY 1995

(IN THOUSANDS OF PERSONS)

	FY 88	FY 89	FY 90	FY 91	FY 92	FY 93	FY 94	FY 95
Total Recipients	1,525	1,563	1,602	1,642	1,683	1,725	1,769	1,813

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Population Research and Family Planning Activities
Obligations Fiscal Year 1987-Fiscal Year 1991
(dollars in millions)

	FY 87	FY 88	FY 89	FY 90	FY 91
TOTAL DHHS	$540.7	$534.3	$550.9	$561.5	$579.6
PUBLIC HEALTH SERVICE					
Office of the Assistant Secretary for Health					
Office of Population Affairs					
Adolescent Family Life Program	1/	1/	1/	1/	1/
Family Planning Program	142.5	137.3	135.1	135.7	135.7 2/
Office of International Health	4/	4/	4/	4/	3/
National Institutes of Health					
National Institute of Child Health and Human Development	132.7	132.9	144.1	150.1	150.1
Office of the Director 5/	.3	.3	.3	.4	.4
Health Resources and Services Administration					
Maternal and Child Health Block Grant	6/	6/	6/	6/	6/
Bureau of Health Professions	38.0	37.2	25.0	4/	4/
Centers for Disease Control	1.7	1.7	1.7	1.7	1.7
Indian Health Service	7/	7/	7/	7/	7/
Total Public Health Service	315.2	309.4	306.2	287.9	287.9

DEPARTMENT OF HEALTH AND HUMAN SERVICES
(continued)

	FY 87	FY 88	FY 89	FY 90	FY 91
OFFICE OF HUMAN DEVELOPMENT SERVICES					
Office of Policy and Legislation	8/	8/	8/	8/	8/
HEALTH CARE FINANCING ADMINISTRATION					
Medicaid Bureau	$225.5	$224.9	$244.7	$273.6	$291.7

Footnotes:

1 The Adolescent Family Life program works to encourage teens not to become sexually active and provides health and social services to pregnant and parenting teens. Family Planning services are authorized in the program only when not available from Title X or other sources in the community.

2 Assumes passage of the Administration's proposal to convert the Title X Family Planning program to a State administered program.

3 All obligations are in excess foreign currency and are not included in the PHS or DHHS totals shown.

4 No obligations are projected for these fiscal years.

5 Represents funds awarded through the BIDs for the Academic Research Enhancement Award program.

6 The Maternal and Child Health Block Grant expends approximately $550 million annually for a broad range of maternal and child health services, including family planning. The proportion of this total allocated to family planning services cannot be determined through available reporting systems.

7 Funding for family planning services cannot be determined.

8 The Social Services Block Grant expends approximately $2.7 billion annually for a broad range of social services, including family planning. The proportion of this total allocated to family planning services cannot be determined through available reporting systems.

GENETIC DISEASES
Obligations

Public Health Service	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
National Institutes of Health	$319,717,000	$358,447,000	$701,465,000	$717,047,000	$743,640,000
Alcohol, Drug Abuse and Mental Health Administration	6,786,000	36,849,000	66,892,000	80,371,000	85,028,000
Health Resources and Services Administration	7,685,000	11,566,000	14,632,000	7,856,000	7,856,000
Total PHS	334,188,000	406,862,000	782,989,000	805,274,000	836,524,000

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NATIONAL INSTITUTES OF HEALTH

National Institute of General Medical Sciences

GENETIC DISEASES

The more than 4,000 known genetic diseases collectively cause widespread suffering. Disorders caused by abnormal genes are thus properly the focus of intense research. In years past, such research was primarily descriptive; little was known about the intricacies of gene function, and clinicians were very limited in the treatments they could offer. Now, scientists manipulate the genetic material, DNA, with increasing ease. This facility has led to improved "gene maps" that show the locations of disease-related genes within the total genetic complement, or genome. Some of these genes, including the ones responsible for Duchenne muscular dystrophy and cystic fibrosis, have been mapped precisely, and now scientists can study in detail how such genes are involved in disease. This knowledge can, in turn, lead to more accurate tests for the presence of genetic disorders and can even open the door to new forms of treatment.

The National Institute of General Medical Sciences (NIGMS) supports basic research aimed at understanding genetic disease and plays a role in making possible many advances in genetics. The research supported by NIGMS often receives national and international recognition, as exemplified by the awarding of the 1989 Nobel Prize in chemistry to grantees Dr. Thomas Cech at the University of Colorado at Boulder and Dr. Sidney Altman at Yale University in New Haven, Connecticut. Other components of the National Institutes of Health, including the National Center for Nursing Research and the Office of the Director, also conduct and support research in genetics.

Fluorescent Technique is Bright Spot in Gene Mapping Effort

The tangled skein of DNA that lies inside each human cell is still mostly terra incognita to the genetic geographers who are working to map its features. Human DNA is divided into 23 pairs of chromosomes, and mapping a gene entails determining the particular chromosome, or region of a chromosome, in which the gene lies. Once a disease-causing gene is mapped to a chromosome, tests to detect its presence can be developed. The more precisely the gene is localized, the more accurate such tests can be. Scientists have mapped with reasonable precision the chromosomal location of about 1,700 genes--a mere 2 percent of the estimated 100,000 genes in the human genome.

Gene mapping is a painstaking procedure. In the nationwide efforts to make a complete map of the human genome, new or improved ways of mapping genes are greeted with interest. This year, NIGMS grantee Dr. David C. Ward at Yale University has introduced a technique that promises to make mapping faster and

more precise. The technique is an improved version of a mapping method called *in situ* hybridization. To map a gene with ordinary *in situ* hybridization, a researcher attaches a radioactive "tag" to a short segment of DNA whose location on a chromosome is unknown. The segment with its tag, called a "probe," is placed on a preparation of a cell's chromosomes.

DNA is a double-stranded molecule composed of subunits (called nucleotides) paired so that each adenine nucleotide is attached to a thymine, while a cytosine nucleotide is always opposite a guanine. Thus, when a probe is placed on specially prepared chromosomes, the probe sticks, or hybridizes, to any place where the nucleotides are complementary to those of the probe. To see where the probe has hybridized, a researcher next covers the sample with a photographic emulsion, and then waits weeks or months for the radioactive tag on the probe to decay and leave a bright spot on the film. The spot corresponds to the location of the probe on the chromosome.

Instead of a radioactive tag, Dr. Ward labels probes with a fluorescent tag that glows immediately after being applied to a sample of chromosomes. Moreover, in contrast to a radioactive molecule, which scatters the particles that are detected on the emulsion into a wide arc, the fluorescent molecule emits light in a straight line. This allows two different probes that have attached very closely to one another on a chromosome to be distinguished.

Thus, most importantly, this improved mapping method permits a researcher to apply several probes to a chromosome at the same time. Each probe can carry a different fluorescent molecule, and each will glow in a different color when viewed with a microscope that combines a computerized optical scanner with a laser that can be "tuned" to detect the various colors of the fluorescent molecules. The speed of the improved technique is such, says Dr. Ward, that in 10 months his group mapped about 600 probes, 10 times as many as could be mapped using radioactive labels.

Genetics and Cancer Connection Clarified

The genetic events that precede the onset of some kinds of cancer have been the subject of intense scrutiny for years. To date, researchers have identified about 50 genes that, if mutated, permit a cell to divide continuously--a hallmark of cancer. These "oncogenes," like most genes, code for the production of proteins, substances that perform most of the work in a cell and that make up its bulk. Just how the proteins made by oncogenes countermand the cell's normal control on growth is not completely understood.

Recently, however, a group of researchers supported by NIGMS discovered an unexpected connection between cholesterol synthesis and the ability of an oncogenic protein seen in colorectal and

pancreatic cancers to trigger cell division. In addition to the cholesterol we get from eating animal products, our bodies also make the substance via a long series of chemical steps. Dr. Jasper Rine and his colleagues at the University of California, Berkeley, used the cholesterol-lowering drug lovastatin to block the formation of a cholesterol precursor called mevalonate in unfertilized frog eggs that contained the human oncogene ras. (Activated ras oncogenes are seen in 90 percent of pancreatic tumors, about 50 percent of colorectal tumors, and between 10 and 20 percent of all other human cancers.)

When mevalonate formation was blocked, the scientists discovered, the protein made by ras was unable to attach to the cell's membrane. If the protein cannot attach, it cannot initiate uncontrolled cell division. This finding is the first to link cholesterol synthesis and the initiation of cancer. It not only helps scientists understand the processes that lead to cancer, it also supports the idea that certain cholesterol-lowering drugs might find a place in the anticancer arsenal. Most importantly, these studies indicate the existence of a heretofore unrecognized enzymatic pathway that could be a target of anticancer drug regimes.

Another group of scientists studying genes and cancer recently found that genetic analysis of colorectal tumor cells can give clues to the probable course of this frequently fatal cancer. The research was led by Dr. Bert Vogelstein at The Johns Hopkins University School of Medicine in Baltimore, Maryland, whose team included two postdoctoral research fellows supported by NIGMS training grants. The scientists examined matched samples of cancerous colon cells and normal colon cells taken from 56 people with colorectal cancer. Using DNA probes, they searched the cells' chromosomes for missing genetic material.

In over 75 percent of the cancerous cells, the researchers found, portions of chromosomes 17 and 18 were missing. In some of the samples, portions of several other chromosomes were also deleted. Moreover, patients with more chromosomal deletion had a poorer prognosis than those people whose chromosome complement was more complete. (For additional discussion of this work, see the National Cancer Institute's submission to the special report on digestive diseases.)

NIGMS grantee Dr. Ronald Evans at the Salk Institute for Biological Studies in La Jolla, California, has also advanced understanding of how oncogenes work. He showed that the oncogenic version of the gene that codes for a thyroid hormone receptor protein blocks the body's normal response to the hormone. Such blockage could mark the beginning of a process that would lead to cancer. This is the first report of an oncogene that inactivates processes that normally control cell growth. The discovery of this new type of oncogene might aid

cancer diagnosis. The presence of the oncogene might, for instance, indicate a risk of developing cancer.

Is Alzheimer's Disease a Result of a Protective Mechanism Gone Awry?

Alzheimer's disease begins in subtle ways, but eventually, people with it lose all their faculties. The cause of this ultimately fatal neurological disorder is unknown, and there is no cure. Although many cases arise spontaneously, up to 50 percent of the cases have a genetic component. This familial form is being studied by NIGMS grantee Dr. Huntington Potter at Harvard University in Boston, Massachusetts, who has uncovered tantalizing new clues about the genesis and progression of Alzheimer's disease.

The brains of elderly persons who have died of Alzheimer's disease are characterized by large numbers of deposits--called plaques--composed of at least two different proteins. Work in Dr. Potter's laboratory is currently directed at understanding the protein called alpha-1 antichymotrypsin (ACT), which, the researchers discovered, is an integral part of the plaques.

ACT is a protease inhibitor produced primarily in the liver. Like all protease inhibitors, ACT hinders the activity of certain enzymes (proteases) whose job it is to break down other proteins. Proteases and their inhibitors exist in equilibrium in many body systems. Whenever proteases begin to work, protease inhibitors are also activated, thereby preventing unchecked protein degradation. Using sophisticated staining techniques, Dr. Potter's group showed that ACT does not enter the brain via the bloodstream, but is produced by certain brain cells.

Next, Dr. Potter measured the amount of ACT messenger RNA (mRNA) in the brains of people who had died of Alzheimer's disease. (Messenger RNA carries instructions for making proteins from the genes to the cell organelles where proteins are manufactured.) ACT mRNA, Dr. Potter discovered, is present in higher-than-normal amounts in the plaques. In other words, there is an "overexpression" of ACT mRNA which, in turn, leads to an excess of the protein.

Dr. Potter's group examined the known functions of ACT for clues to its role in Alzheimer's disease. Liver ACT production increases in response to such circumstances as infection or inflammation. Perhaps, the scientists suggest, a similar increase in ACT occurs in the brain following a cellular injury there. Ordinarily, the level of a protease produced in response to injury or inflammation decreases as the system returns to normal. However, in Alzheimer's disease, this return to the status quo may not occur. Instead of protecting the brain from uncontrolled protein breakdown, an overzealous response by ACT may contribute to the development of Alzheimer's disease.

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National Cancer Institute

This year, the National Cancer Institute (NCI) and NCI-funded scientists contributed to advances in genetics research by conducting the first approved gene transfer experiments in humans and by mapping certain cancer genes and characterizing their functions.

Preliminary Gene Transfer Study Results Announced

In the gene transfer study, intramural scientists Drs. Steven Rosenberg and Michael Blaese, with Dr. French Anderson at the National Heart, Lung, and Blood Institute, transferred cancer-fighting cells containing "foreign" genes into patients with advanced melanoma--a deadly type of skin cancer. The cancer-fighting cells, called tumor infiltrating lymphocytes or TIL's, are removed from the patients' tumors and multiplied with the growth factor interleukin-2 (IL-2). When transferred, with more IL-2, back to the patients, TIL's home in on the tumor from which they are derived. The foreign gene acts as a marker; it does not have a therapeutic effect. In September 1989, Dr. Rosenberg reported preliminary results that all five melanoma patients who received the gene-transferred TIL's had tolerated the cells thus far, with no side effects from the transferred foreign gene. The modified cells survived for more than 19 days.

Gene for Melanoma Localized

In other research, intramural scientists Drs. Sherri Bale and Margaret Tucker, former NCI intramural scientist Dr. Mark Greene (now at Arizona Medical Center in Peoria), and colleagues located the gene for familial melanoma on the short arm of chromosome 1. Familial melanoma accounts for about 10 percent of all melanoma, a form of skin cancer whose incidence is increasing rapidly. This discovery provides a starting point for identifying the specific gene for the disorder and characterizing its function.

Site of Childhood Cancer Gene Determined

Most cases of kidney cancer in children are Wilms' tumors. These cancers are associated with congenital abnormalities due to deletions in chromosome 11. NCI intramural scientist Dr. Frederick Li and colleagues, collaborating with Drs. Paul Grundy and Webster Cavenee at the Ludwig Institute for Cancer Research, Royal Victoria Hospital, Montreal, Canada, have found that the gene for familial predisposition to Wilms' tumors is not located on chromosome 11, but is in another location that, when mutated, is capable of conferring an inherited predisposition to Wilms' tumor.

National Heart, Lung, and Blood Institute

Research on genetic diseases supported by the National Heart, Lung, and Blood Institute (NHLBI) focuses on inherited disorders of the heart, blood vessels, lungs, and blood.

Transgenic Mouse Model Makes Human Hemoglobin

In a development that opens new avenues for research on sickle cell disease and other blood diseases, scientists have created laboratory mice whose blood cells make human hemoglobin. Dr. Tim M. Townes, a grantee at the University of Alabama at Birmingham, and his team implanted normal human hemoglobin genes into mouse embryos. The embyros grew to adult mice whose genes made the correct amount of hemoglobin. The investigators plan to use similar methods to implant defective genes, such as those that cause sickle cell disease or other hemoglobin disorders. If they are successful, researchers will have, for the first time, animal models of these diseases, enabling them to study the disorders in greater detail and to try experimental treatments that would be impractical or unethical to attempt in humans.

Genetic Assay and Transgenic Mouse Model Developed for Protein Deficiency Associated with Familial Emphysema

A group of diseases of the lung, collectively referred to as emphysema, are associated with progressive destruction of certain lung cells and eventual failure of the lung's ability to exchange gases (oxygen and carbon dioxide). Familial emphysema is associated with a hereditary deficiency of the enzyme alpha-1 antitrypsin (AAT). Normally, AAT inhibits the action of another enzyme in the lungs. A deficiency of AAT allows the other enzyme to destroy the lung cells.

Recently, Dr. Ronald Crystal, an NHLBI intramural researcher, added nine examples to the list of known mutations that lead to AAT deficiencies, the most common form of which is the Z mutation. An assay was developed to screen patients for the Z mutation, which reveals the mutation even in the absence of clinical signs of disease. Further, in a step toward therapy, mouse cells engineered to produce AAT were transplanted into mice. The cells raised the AAT levels in the blood and lung fluids of the mice.

The lack of an animal model of AAT deficiency has impeded the study of this disorder. To address this need, NHLBI initiated a contract program to develop a genetically engineered animal model of the AAT-deficient human. Under the contract, Dr. Douglas Hanahan at the Cold Spring Harbor Laboratory in Cold Spring Harbor, New York, and Dr. Joseph A. Sorge at the Research Institute of Scripps Clinic in La Jolla, California, developed mice that carry the mutant human AAT gene. The animals display many of the changes seen in AAT deficiency in human newborns.

National Institute of Dental Research

The National Institute of Dental Research (NIDR) supports research on the genetic bases of cleft lip and palate, inherited dysplasias (abnormal development) involving the teeth and bone, and periodontal diseases.

Research Enhances Understanding of Amelogenesis Imperfecta (AI)

NIDR grantees Drs. Eduardo Lau, Malcolm Snead, and Harold Slavkin of the University of Southern California, Los Angeles, discovered that amelogenin, the human gene for tooth enamel, is located on the human X, as well as the Y, chromosome. This will help understanding of a major form of AI that is inherited as an X-linked (passed through the maternal line) defect.

Basic Research Underpins Clinical Study of Dysplasia

Intramural scientists Drs. John Termine and Pamela Gehron Robey are working with Dr. Ulrich Vetter of the Federal Republic of Germany to characterize the matrix proteins in people with the bone disorder osteogenesis imperfecta. This work may help identify the developmental defect involved in the disease.

Collaboration with Industry Moves Bone Studies Forward

Using new techniques, intramural scientist Dr. Hari Reddi and colleagues have collaborated with a biotechnology firm to achieve recombinant cloning of osteogenin and other bone-inducing proteins, which will ultimately reduce the need for grafted bone.

Researchers Advance Knowledge on Cleft Lip and Palate

Dr. David L. Gasser, an NIDR grantee at the University of Pennsylvania in Philadelphia, and his colleagues have mapped the gene for cleft palate susceptibility within a small section of chromosome 17 of specially bred mice. Also, NIDR grantee Dr. Jeffrey C. Murray and colleagues at the University of Iowa in Iowa City have shown that transforming growth factor-alpha is associated with the most common form of cleft lip and palate.

NIDR grantee Dr. Michael Melnick and colleagues at the University of Southern California analyzed data on 1,000 families with cleft lip and palate in Shanghai, China, and showed that the best-fitting inheritance pattern is that of an autosomal recessive major gene. Family data collected in the Philippines by Dr. Chin S. Chung, an NIDR grantee at the University of Hawaii at Manoa, Honolulu, suggest that the genetic bases are multifactorial and differ between Caucasians and Filipinos.

National Institute of Diabetes and Digestive and Kidney Diseases

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducts and supports genetics research on a variety of metabolic and hormonal disorders that are known or suspected to be hereditary. NIDDK grantees recently announced the identification of the cystic fibrosis gene, a long-awaited breakthrough, which is discussed separately in the report on cystic fibrosis.

Gene Defect Found in Adult Tay-Sachs Disease

The adult form of Tay-Sachs disease, like the infantile form, is characterized by an enzyme deficiency that leads to degenerative changes in the nervous system. Ashkenazi Jews are at particular risk of developing this hereditary disorder. In the adult form, which is less severe, symptoms, often including psychosis, begin in the second or third decade of life. NIDDK's Dr. Richard Proia led a group of scientists that identified the gene defect that causes adult Tay-Sachs. Their finding, together with two previously identified infantile Tay-Sachs gene mutations, will allow for more accurate genetic screening.

Susceptibility to Diabetic Nephropathy May Be Genetic

The kidney disease of diabetes is the most common cause of end-stage renal disease in the United States, accounting for 30 percent of new patients who enter therapy for end-stage renal disease. Why some people with diabetes are prone to nephropathy, while others are not, has intrigued investigators. Many believe that high blood pressure and poor blood sugar control lead to nephropathy, but others have turned their attention to the role heredity may play in the disease. NIDDK grantees Drs. Elizabeth Seaquist, Frederick Goetz, and Jose Barbosa at the University of Minnesota in Minneapolis studied two families and found that diabetic nephropathy occurs in familial clusters. This discovery is consistent with the heredity hypothesis, but further studies are necessary to rule out the possible influences of environmental factors shared by siblings.

Drug May Lessen Severity of Sickle Cell Disease

NIDDK scientists Drs. Griffin Rodgers, Connie Noguchi, and Alan Schechter have found that the drug hydroxyurea reduces some of the complications of sickle cell disease, a devastating hereditary blood disease that is often treated with blood transfusions. The drug "turns on" fetal hemoglobin genes, which raises the level of this type of hemoglobin (normally produced only during fetal life). The investigators found that when the drug was given to people with sickle cell disease, the total blood count increased, suggesting that fewer blood transfusions will be necessary with longer-term treatment.

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National Institute of Neurological Disorders and Stroke

The brain and nervous system are profoundly susceptible to damage resulting from genetic defects because an estimated 30 to 50 percent of human genes are expressed solely or mainly in the brain. The National Institute of Neurological Disorders and Stroke (NINDS) supports and conducts research into neurogenetic diseases, with the goal of developing effective means to prevent or treat these disorders.

Overcoming Lipid Storage Disorders

Lipid storage diseases are genetic diseases in which complex lipids (fats) fail to undergo enzymatic breakdown, and are deposited in body tissues. This lipid accumulation may cause numerous neurological and physiological abnormalities, and, sometimes, premature death. Gaucher's disease is caused by a defect in the gene that directs production of the enzyme glucocerebrosidase. NINDS intramural scientists Drs. Roscoe Brady and Norman Barton recently treated one child who has Gaucher's disease with weekly infusions of glucocerebrosidase--a pioneering strategy called enzyme replacement therapy. Within 4 months, the child's severely low hemoglobin level rose to nearly normal. Removal of the child's spleen, imminent prior to the enzyme therapy, was avoided. Another NINDS intramural scientist, Dr. Stefan Karlsson, has employed gene transfer techniques to implant the human glucocerebrosidase gene into mice. Bone marrow was removed from the mice, treated with a growth factor to stimulate cell division, and exposed to an inactivated virus containing the human gene. The mouse bone marrow cells then produced human glucocerebrosidase. This is an important step in developing gene replacement therapy for Gaucher's disease.

The lipid storage disease Niemann-Pick Type C (NPC) is characterized by the abnormal accumulation of cholesterol inside cells. A team of NINDS scientists led by Dr. Peter Pentchev recently used dimethyl sulfoxide (DMSO) to reverse cholesterol buildup in cultured cells taken from people with NPC. NINDS clinicians have begun a study to test the effectiveness of DMSO in people with NPC.

Demystifying Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a genetic neuromuscular disease that causes progressive muscle weakness and, eventually, death in those people (always males) who inherit it. Several years ago, NINDS grantee Dr. Louis Kunkel at Children's Hospital in Boston, Massachusetts, located the DMD-causing gene, and later identified dystrophin, the protein whose absence results in the disease's symptoms. Recently, Dr. Kunkel collaborated with British scientists to treat DMD in a mouse model of the disease.

They transplanted normal muscle precursor cells into the affected animals. Tissue analysis later revealed that the transplanted precursor cells fused with diseased muscle fibers, producing dystrophin and opening the way toward reducing the animals' symptoms. Another NINDS grantee, Dr. Peter Law at the University of Tennessee in Memphis, has taken preliminary steps toward testing the mouse model cell transplant technique with human donors and patients.

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National Institute of Allergy and Infectious Diseases

Research supported by the National Institute of Allergy and Infectious Diseases (NIAID) investigates the genetic basis of immune system diseases.

Details of Chronic Granulomatous Disease Emerge

Chronic granulomatous disease (CGD) is an inherited disease that usually develops during early childhood. Affecting about one in a million people, CGD leaves one vulnerable to serious infection by bacteria and fungi. NIAID intramural researchers Drs. Harry Malech, John Gallin, and their colleagues, in collaboration with NIAID grantees Drs. Bryan Volpp, William Nausef, and Robert A. Clark at the University of Iowa, recently determined the defects underlying two newly discovered forms of CGD. By analyzing these defects, the scientists are moving closer to developing treatments for CGD based on protein replacement or gene therapy.

The NIAID team set out to determine the exact abnormalities in a group of people with CGD who inherited the disease in a pattern known as autosomal recessive; people with this pattern make up about one-third of all people with CGD. The researchers determined that abnormalities in at least two different proteins found in the cytosol (the material outside the cell's nucleus) resulted in the autosomal recessive form of CGD.

More recently, Dr. Malech and his colleagues cloned the gene that encodes one of these proteins, which they named NCF-47k. Cloning the gene allowed the scientists to prepare a recombinant form of the protein, which they used to study a protection system, called the respiratory burst, that occurs in immune cells known as phagocytes. Upon ingesting bacteria or fungi, a normal phagocyte produces hydrogen peroxide, which helps other proteins in the phagocyte kill the microorganism. The researchers confirmed NCF-47k's critical role in the respiratory burst by mixing the recombinant protein with defective cells in test tubes. Adding the protein to the defective cells caused the respiratory burst to occur. The ability of recombinant NCF-47k to correct the defect in cell culture gives scientists hope that the protein might be used as a medicine to treat people who have CGD. But there are currently limitations to that form of therapy.

Meanwhile, scientists can begin using the cloned NCF-47k gene to analyze the genetic material of people with CGD in order to identify the defective gene and determine its abnormalities exactly. In addition, understanding the biological mechanisms that underlie the respiratory burst may lead to therapies to improve this important immune defense system in people, such as older individuals, who are susceptible to infections.

National Institute of Child Health and Human Development

The National Institute of Child Health and Human Development (NICHD) funds a number of projects to study heredity and its variation. Newly developed techniques are helping scientists to understand what specific genes do, and how and when they affect development--the key to detecting and preventing serious genetic diseases.

Down Syndrome Studied in Animal Model

Last year, NICHD grantee Dr. Yoram Groner at the Weizmann Institute of Science in Rehovot, Israel, continued his research on Down syndrome, the most common genetic birth defect associated with mental retardation. The condition occurs in 1 of every 1,000 births, and a woman's chance of having a baby with Down syndrome increases significantly once she reaches the age of 35. The condition has been associated with congenital heart disease, susceptibility to infections, and a high cancer rate, as well as numerous characteristic physical features. The syndrome has been attributed to the presence of an extra copy of chromosome 21. By introducing clones of chromosome 21 into mouse genes, Dr. Groner has been able to produce some of the features of Down syndrome in an animal model. As his studies continue, he may be able to tell which gene or genes on chromosome 21 are responsible for the various physical, anatomical, and biochemical abnormalities of the disease.

Autoimmunity and Learning Disability Connection Explored

Dyslexia is a term used to indicate a variety of reading, writing, and learning disorders. NICHD grantee Dr. Albert Galaburda at Harvard University used a mouse model to explore areas of the brain that may be involved in congenital learning disabilities. To test the theory that an autoimmune disease (a disease resulting from the body's production of antibodies against its own tissues) is responsible for causing dyslexia in humans, Dr. Galaburda is cataloging the differences between the right and left sides of the brain in normal and immune-deficient mice. In addition, he is studying the brains of dyslexic humans to determine whether anomalies found in humans are similar to those found in animal models.

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National Eye Institute

Retinitis pigmentosa (RP) is a group of inherited retinal degenerations that affects young adults. RP types differ in inheritance pattern, time of onset, severity, and progression, but all have the same end stage--blindness. Currently, there is no cure or treatment for the estimated 100,000 Americans who have RP. The National Eye Institute (NEI) supports research on the causes of genetic eye disorders, particularly retinal diseases such as RP.

Dog Model Provides Important New Clues to the Cause of RP

Initially, RP affects retinal cells called rods, which provide night and side vision. Next to deteriorate are the cones, which are responsible for fine, central vision and for color vision. Eventually vision deteriorates to severe visual impairment or blindness, often before the person reaches age 40.

Research on RP has been difficult because human donor tissue is scarce and often comes from people with end-stage disease. Cell cultures cannot show disease progression. Now, in a strain of miniature poodles that naturally develops a blinding RP-like degeneration, scientists have found a metabolic error outside of the retina that disrupts the supply of a fatty acid essential for rod cell stability.

High levels of the fatty acid docosahexaenoic acid, or 22:6, are normally found in rod outer segments, suggesting that it is critical to rod function. The first observable deterioration in RP occurs when replacement of rod segments begins to slow.

To investigate the traffic patterns of basic nutrients in the eyes of affected dogs, NEI scientist Dr. Paul O'Brien and his associates injected a mixture of fatty acids into the dogs' eyes. The scientists found that one, the precursor to 22:6, became incorporated into the rod lipids, but it did not convert to 22:6 as expected. This was true for both the affected and normal dogs, suggesting that some other organ is the natural source of 22:6. Moreover, the affected dogs had low levels of 22:6 in their blood plasma, which could explain why this fatty acid, which is normally damaged by oxidation, is not replenished. Although many questions remain about what is causing the defect, this dog model has provided the first clue that the cause of a retinal degeneration may lie outside the retina. The scientists now plan to feed the dogs a supplement of 22:6 to test whether it will correct the underlying defect and prevent blindness.

Humans who have certain inherited forms of RP also have abnormally low plasma levels of 22:6. If the affected dogs respond to dietary supplementation, the scientists believe that these RP patients may also benefit from a similar therapy.

National Institute on Aging

As they age, cells lose the ability to reproduce. In addition, a variety of structural and metabolic changes occur. Researchers supported by the National Institute on Aging (NIA) are studying age-related changes in the duplication of DNA (called replication) necessary for cell reproduction as well as the "turning on" (expression) of genes in an effort to find both the causes of cellular aging and ways to retard human aging.

Immortalized Cells Offer Clues to Cellular Aging

Normally, cells divide only a certain number of times and then stop. By comparing mortal cells (those that age and die) with immortal cells, researchers hope to learn what controls cellular aging. (Immortal cells have been genetically altered so they proliferate endlessly; that is, they do not age.)

NIA grantee Dr. Olivia M. Pereira-Smith at Baylor College of Medicine in Houston, Texas, is studying what happens when mortal and immortal cells are fused. She found that hybrids have limited division potential, and thus behave more like mortal cells than immortal ones. One theory to explain this finding is that aging results from a program that includes the expression of a gene whose product inhibits DNA synthesis. Immortal cells may not age because they lose their ability to respond to this gene product; thus, they escape the genetic program for aging. Further research involving immortalized cells should provide additional information about how programmed aging is controlled and whether this process can be reversed.

Gene Expression May Control Aging Cells' Biological Clock

Scientists wish to explain why normal cells appear to possess a biological memory, or clock, which determines their average lifespan. Some researchers believe that this clock may be triggered by an event that occurs within the cell. NIA grantee Dr. Eugenia Wang of the Lady Davis Institute for Medical Research and McGill University in Montreal has identified such an event. She has found that proliferating cells produce a protein called cyclin, but they lack the protein statin. In contrast, aging cells contain statin, but not cyclin. The structure of statin suggests that it may interfere with protein synthesis.

Dr. Wang observed that these protein changes also occur during cell differentiation, the series of changes that cells undergo to form a specialized tissue. These proteins appear to mark the transition from a proliferating to a non-proliferating, or quiescent, state. Statin is a marker for quiescence in a number of organisms and is thus a possible "marker of aging."

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National Institute of Arthritis and Musculoskeletal and Skin Diseases

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) supports and conducts research on the genetic mechanisms that influence normal development and on diseases of the bones, joints, skin, and connective tissue.

Gene for Key Allergy Protein is Cloned

A landmark accomplishment in allergy research was made by NIAMS intramural researchers who used a rat model to determine the genetic structure of a key protein involved in triggering allergic reactions. This finding gives researchers their first opportunity to search for drugs to prevent allergy attacks rather than just control the symptoms. Research has been hampered because human cells that have this protein, called the IgE receptor, are scarce and difficult to purify. Drs. Henry Metzger and Jean-Pierre Kinet, however, were able to clone and sequence the gene for the IgE receptor. They have applied the knowledge about the rat receptor to generate some parts of this protein in humans. The scientists are working with a pharmaceutical company to identify drugs that block the receptor and halt allergic reactions.

Cloned Vitamin D Receptor Gene May Help Understanding of Rickets

NIAMS grantees Dr. Mark Haussler at the University of Arizona, Tucson, and Dr. J. Wesley Pike at Baylor College of Medicine have cloned and determined the sequence of the gene for the receptor protein for human vitamin D. Vitamin D regulates the absorption of calcium and influences the mineralization of bone. This work provides researchers with a new opportunity to study how vitamin D regulates normal bone development and to further explore diseases, such as vitamin D-dependent rickets, in which the vitamin D receptor is abnormal.

Psoriasis Study Indicates Role for Growth Factor Gene

NIAMS grantee Dr. James T. Elder at the University of Michigan, Ann Arbor, and colleagues have shown that the regulation of a key growth factor may be involved in the skin disorder psoriasis. Psoriasis is a chronic disease in which skin cells mature very rapidly and cause a buildup of dead cells on the skin's surface.

Dr. Elder examined the gene expression of two growth factors in the skin, one that promotes skin cell growth and one that inhibits growth. He and his colleagues found that, compared to normal skin, psoriatic skin produced excess amounts of the factor

that encourages cell growth. This suggests that, in psoriasis, the regulation of the gene for the skin cell growth-promoting factor may be faulty.

More findings on genetic mechanisms can be found in the report on arthritis, rheumatic diseases, and related disorders.

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National Institute on Deafness and Other Communication Disorders

The National Institute on Deafness and Other Communication Disorders (NIDCD) conducts and supports research and training on disorders of hearing and other communication processes, including diseases affecting hearing, balance, voice, speech, language, taste, smell, and touch.

Genetic Underpinnings of Deafness Explored

Approximately 50 to 60 percent of deafness/hearing impairment present at birth or in early childhood is genetic. The impact of heredity upon late-onset hearing disorders is mostly unknown, but it is believed to be considerable. Because of the significant role of genetic factors in causing hearing impairment or deafness, NIDCD is supporting ongoing research in this area. Significant progress has been made in mapping the genes of the few X-linked disorders involving hearing loss (Norries disease, perilymphatic gusher, and Alport syndrome). Recent advances in genetics and molecular biology have opened an opportunity for research that should lead to an understanding of how hearing impairment and deafness are transmitted from parent to offspring. Such studies should also do much to clarify the biology of hearing and the molecular nature of its disorders.

The mapping of genes that cause deafness or other types of hearing impairment and the characterization of such genes and their protein products are high priority areas of science for NIDCD. Advances in these areas can be achieved through the study of large families with members who have inherited deafness, by the study of genes involved in the manufacture of auditory structures in the human inner ear and brain, and also through the study of animal models of genetic deafness. These and other methods may lead to the cloning and decoding of genes that cause deafness. Means of earlier diagnosis and more precise methods of genetic counseling and medical management can then be developed. Ultimately, genetic engineering techniques may allow the correction of hearing impairments.

Hereditary Hearing Loss in Mice Studied

Many gene mutations cause hereditary hearing loss in mice. NIDCD intramural scientists are particularly interested in the mouse strain called the Bronx Waltzer because it has an autosomal recessive mutant gene that has been implicated in changes in the auditory system. In the cochlea of mice that have two copies of the mutant gene, most of the inner hair cells disappear during development and the few remaining hair cells do not develop normally. The outer hair cells, however, show little pathology. The NIDCD researchers are now seeking to map the gene to its chromosome.

Division of Research Resources

The Division of Research Resources (DRR) supports and conducts research into a wide variety of genetic diseases at shared research facilities across the United States. General Clinical Research Centers (GCRC's) provide the research infrastructure for multidisciplinary studies on both children and adults. Specifically, they provide patient research facilities, computerized data management and analysis, as well as research nurses, dietitians, biostatisticians, and specialized laboratories for the translation of basic and clinical research into medical practice.

Four People with CGD Treated with Gamma Interferon

Recently, Dr. Stuart Orkin and other DRR grantees at the Children's Hospital GCRC in Boston, Massachusetts, isolated and cloned the gene responsible for the white blood cell defect seen in chronic granulomatous disease. Study of the cloned gene led to the identification of a protein that is absent in the white blood cells of people with CGD.

The DRR grantees also found that gamma interferon activates immune cells by turning on the production of this missing protein. Based on these tests, Dr. Orkin and his associates injected recombinant gamma interferon into four people with the disease. Immune function improved to normal in two of the four. According to Dr. Orkin, the study provided the basis for a clinical trial of the drug, which is currently under way. (This research is also supported by NICHD.)

Early Diagnosis of Gaucher's Disease is Now Possible

Gaucher's disease is being studied by Dr. Ernest Beutler and other DRR grantees at the Scripps Clinic GCRC in La Jolla, California. They have cloned the DNA that codes for glucocerebrosidase, the enzyme absent in Gaucher's disease. This has for the first time enabled investigators to diagnose the condition on a molecular level using DNA sequence analysis.

Using clinical data and DNA samples from 50 patients with Gaucher's disease, the grantees identified a specific genetic mutation on a DNA segment. According to Dr. Beutler, this knowledge will allow clinicians to predict the severity of the clinical course in children with Gaucher's disease, even when they are diagnosed at a very young age.

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OUTLOOK

Each year, scientists who search the innermost workings of cells for clues to the origins of genetic disease move closer to the knowledge needed to combat these devastating illnesses. This year is no exception. Undergirded by basic research that uses cell cultures, molecular biological techniques, and animal models of disease to study normal and abnormal conditions, NIH scientists and grantees are moving in ever larger steps toward better diagnosis, prevention, and, eventually, cures for genetic diseases.

ALCOHOL, DRUG ABUSE AND MENTAL HEALTH ADMINISTRATION

National Institute of Mental Health

GENETICS RESEARCH

Background

Genetic linkage strategies provide a way to test the hypothesis that a gene, or genes, underlie susceptibility to particular disorders. The concept of genetic linkage in psychiatric disorders has been controversial because these illnesses are clinically, behaviorally, and biologically complex. Nonetheless, examples from the general medical literature demonstrate that even a single gene defect can have disastrous effects, and that the same illness can be produced by different genes (genetic heterogeneity). The complexity of psychiatric illnesses does not preclude the possibility that they have genetic components.

If a piece of DNA can be identified as it is passed on from parent to child, one can then determine if that segment of DNA is linked to an illness. A particular piece of DNA is linked to an illness if the marker is typically present when someone is ill. If a piece of DNA is linked, the gene in question must be close to that piece of DNA. In the past, there was no method of labeling each piece of DNA, thus limiting linkage studies. The development of highly informative chromosomal markers--essentially clear road signs placed throughout the whole genome--has been the critical breakthrough.

Because of these developments, the Decade of the Brain (the 1990s) will also be a period of unprecedented related progress in genetics. To capitalize on this scientific opportunity, there is a need to develop a resource of families available for study. The National Institute of General Medical Science (NIGMS) Cell Repository is an example of an initiative which has successfully provided the general medical field with the clinical material to pursue genetic studies. However, because of important diagnostic concerns in the psychiatric disorders, there is a need for NIMH coordination of such an initiative. The use of valid and reliable diagnoses, consistent methods, and potential latent markers in a large national sample will minimize the potential role of diagnostic procedural or criteria differences in these studies.

NIMH Initiatives

The National Institute of Mental Health (NIMH) has launched an initiative to study the molecular genetics of severe mental illnesses. The first facet of this initiative is the Diagnostic Centers for Psychiatric Linkage Studies program. In September of 1989, NIMH entered into a cooperative agreement with ten centers at Columbia, Washington, Harvard, Johns Hopkins, and Indiana Universities as well as Massachusetts General Hospital, the

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University of Alabama-Birmingham, and the NIMH Intramural Research Program. By coordinating the diagnosis of patients and their family members across all of the centers, this program will establish a national resource of cell lines from individuals with schizophrenia, manic-depressive illness, and Alzheimer's disease. This large undertaking will be a major step toward understanding the complexity of inheritance in these three disorders.

The molecular genetics initiative will also include a National Pedigree Research Service. This second facet will focus on large pedigrees, families with many ill members. This approach to molecular genetic linkage has proven the most fruitful so far with recent reports from throughout the world having already provided some very significant findings. The Service, now under development, will provide technical assistance and financial support for the careful and rapid study of these important families regardless of where they may live.

These two programs will be closely coordinated with the NIMH intramural program, and staff will work closely with a number of independent research centers already supported by NIMH to focus this new technology on mental illnesses, some of the most severe public health problems facing the nation.

Recent Findings

Recent findings have fueled the enthusiasm for applying molecular genetic methods to the study of psychiatric disorders while also demonstrating the complex nature of this type of research.

Research into schizophrenia has demonstrated linkage to chromosome 5 in seven families. This is a major first step. Findings that some families do not show this linkage are consistent with the belief that there are multiple genetic causes for schizophrenia.

The first reports of genetic linkage were made in 1987 in a large family with manic-depressive illness. Follow-up studies looked for this reported linkage to chromosome 11 and also reported linkage to the X-chromosome in several other families. However, NIMH intramural scientists in the Clinical Neuroscience Branch recently reported new evidence casting doubt on the likelihood that a gene located on chromosome 11 is linked to manic-depressive illness in the Old Order Amish. The negative finding followed the discovery by molecular geneticists that the gene for tyrosine hydroxylase, the enzyme that makes dopamine, was not the suspect gene on chromosome 11 for manic-depressive illness. Investigations are continuing on other possible genetic markers for affective disorders and schizophrenia utilizing an expanded collection of genetic material from large affected families for these studies.

The extramural Division of Clinical Research is also actively supporting a number of studies with major genetics aspects. It currently funds eleven genetics grants in the area of

schizophrenia, six of which focus on molecular genetics, three of which examine twins, and two of which study epidemiology. Two of these grantees are studying both schizophrenia and manic depressive illness. Among other NIMH grants focused on mood, personality, and anxiety disorders are eight which place a major emphasis on molecular genetics and ten which examine family aggregation and the transmission of biological markers in families with mood disorders. The Epidémiology and Psychopathology Research Branch is also funding 12 grants with major genetic aspects.

The genetic mechanisms that control dopamine systems of the brain are now the focus of intense investigation. Earlier evidence indicated dopamine involvement in many severe neuropsychiatric disorders such as psychosis and schizophrenia. Studies now focus on the molecular biology of dopamine gene expression and regulation utilizing techniques ranging from culturing nerve cells in order to study the dopamine receptor in isolation to using animals with an altered genetic makeup.

Karen O'Malley (Washington University) is studying the physiological role of the dopamine synthesizing enzyme, tyrosine hydroxylase (TH). She is able to insert the TH gene via a retrovirus vector into specific cell lines in order to study the mechanisms that control the expression of that TH gene.

The specific anatomical difference between the dopamine-containing systems of two specific brain areas, the substantia nigra and ventral tegmental area is also of interest. These two systems are implicated in movement disorders and psychiatric disorders, respectively. Suzanne Roffler-Tarlov (Tufts University) is investigating the genetic control of these two distinct anatomical dopamine systems in a strain of mutant mice. These mutant mice have abnormalities of dopamine synthesis in the substantia nigra but not in the ventral tegmental neurons. By studying the expression of the TH gene in both anatomical systems, she will gain information on the distinguishing features of abnormal TH gene regulation.

Another project is studying the gamma-amino butyric acid (GABA) producing neurons of the striatum and substantia nigra (Marie-Francois Chesselet, Medical College of Pennsylvania). GABA neurons interact with dopamine neurons in these nuclei. They are believed to be an important participant in the pathophysiology of psychiatric disease. This study focuses on the GABA synthetic enzyme glutamic acid decarboxylase (GAD). Dr. Chesselet is investigating the effects of lesions placed in the striatum or substantia nigra, which alter dopaminergic transmission. The effects of this are then studied in terms of the regulation of the GAD gene expression by measuring GAD messenger RNA levels.

The aforementioned studies of the dopamine system, along with research being conducted by intramural investigators, are designed to increase understanding of the molecular biological mechanisms involved in the activities of neurotransmitters (and the expression

of their genes) that play important roles in the development of several psychiatric disorders including schizophrenia and depression. In their efforts to unravel the workings of brain chemical messenger systems, investigators are making discoveries that promise a new generation of treatments based on an in-depth knowledge of how psychoactive drugs produce their effects.

Bruce Pennington (University of Denver) has utilized recent advances in genetic linkage and complex segregation analyses to examine dyslexia. Both genotype and phenotype analysis in dyslexia are complicated by the fact that dyslexia is a disorder in which both causal heterogeneity and heterogeneity of observable characteristics are likely. Pennington has identified groups of dyslexic subjects that are homogeneous with respect to cause: the members of one group have an apparently autosomal dominant form of familial dyslexia (i.e., the offspring of a dyslexic have a 50 percent chance of developing the disease) which is linked to chromosome 15, while preliminary results in another group suggest a second major locus on chromosome 6. The identification of an etiologically pure subtype through linkage analysis has advantages in terms of greater phenotypic specificity and future possibilities of prevention. This finding, taken with others, also suggests that there are important relationships among various types of psychopathologies. There is preliminary evidence for connections between familial subtypes of dyslexia and clinical correlates (e.g. depression, Attention Deficit Disorder, and immune disorders) by virtue of gene-site proximity. Longitudinal and other types of analyses of these clinical correlates of dyslexia will help determine which are causally related to the dyslexic phenotype(s), and in what way.

The familial form of Alzheimer's disease is also being studied with molecular genetic methods and was one of the first illnesses to be linked to a particular location (locus) on the genome. At present, genes are the only causal factor conclusively identified and, thus, provide the only confirmed clue to unraveling the mystery of this disease.

One of the characteristic pathological changes found in the brains of AD patients after death is neuritic plaque, a focal collection of degenerating nerve endings surrounding a core of "amyloid" protein. Plaques and other hallmarks of the disease occur primarily in the brain regions associated with higher cognitive functions (i.e., learning and memory). These areas are the cerebral cortex, the hippocampus, the amygdala, and some deep brain areas, particularly the basal nucleus.

One of the most exciting aspects of current research on AD is the attempt to identify the chemical structure, source and pathogenesis of the fibrous proteins that characterize the plaques. This line of inquiry has shown great promise for elucidating genetic mechanisms of the disease and, potentially, for leading to clinical interventions. Evidence supports the conclusion that both the vascular and plaque amyloid of AD have the same principal

component, which is a beta-protein. Whether this protein is produced in the brain or in another body organ remains unknown. Studies have revealed that the beta-protein is made up of fragments of a larger protein molecule that normally spans the nerve cell membranes. Since preliminary data indicate that the gene coding for this beta-protein is in all the cells of the body, scientists are asking why it should be selectively expressed in the brains of AD victims. Molecular genetic techniques have been employed to study the origins of amyloid in both familial AD (cases occurring with a significant family history of AD in ancestors) and sporadic AD (cases without such a family history).

Several investigators have located the amyloid protein gene on chromosome 21 adjacent to a region associated with Down syndrome, a developmental disorder of genetic origin. This common genetic base on chromosome 21 provides a rationale as to why individuals with Down's syndrome who reach 40 years of age develop Alzheimer-like neuropathologic changes. Other research has provided evidence that a significant excess of Down's syndrome births occur in families identified by of a case of AD.

Additional markers linked to familial AD have also been identified on chromosome 21. Despite initial hopes that the two genes might be more closely linked, the most recent molecular studies have shown that the marker gene for familial AD and the gene for beta amyloid protein are not identical but reside at separate points on chromosome 21.

The molecular genetic findings on familial AD have been based primarily on information pooled from several families showing a large number of AD cases and an autosomal dominant pattern of inheritance, which means that offspring of an AD patient have a 50 percent chance of developing the disease. Additional such families, participating in the Diagnostic Centers for Psychiatric Linkage Studies program, will constitute an important resource for researchers attempting to identify, through molecular genetic approaches, the gene responsible for AD.

Along the same lines, a previously funded project has been establishing lymphoblastic cell lines on all available members of at least five families which are affected by autopsy-proven diagnoses of AD in a pattern consistent with transmission by an autosomal dominant gene. These cell lines can be used as a permanent source of DNA from each family member and will allow identification and characterization of the DNA sequence critical in AD. This methodology can be extended to additional families with large numbers of Alzheimer's patients as they are identified. Although the pace of discovery in molecular genetics has been rapid, the prospective collection of tissue samples should accelerate further the identification of the gene(s) involved in AD. As new technologies become available, they can be applied immediately to these multi-generational samples rather than having to wait for a new generation of patients to develop confirmable AD. The advances being made may lead to the discovery of a diagnostic

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marker for early stages of AD and to clinical interventions to slow or halt the disease.

As the above findings indicate, genetics research has already produced important results. In the coming years, its importance will grow as it holds great promise for elucidating answers to some of the most puzzling questions about mental disorders.

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National Institute on Alcohol Abuse and Alcoholism

GENETICS

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) supports both extramural and intramural research into the genetics of alcoholism. Alcoholism appears to be a disorder involving the interaction of genetic, behavioral, psychological, and sociocultural determinants. Recent advances in the classification of subtypes of alcoholism, the identification of biological markers of alcoholism, and the mapping of the human genome through the use of recombinant DNA techniques are allowing genetics research on alcoholism to progress, and it should soon be possible to isolate genetic factors important in the etiology of this disorder.

Evidence of a genetic influence in the etiology of alcoholism has come from studies of alcoholism in families with multiple cases, in identical versus fraternal twins, and in adoptees separated from their biological parents at an early age. Animal lines bred for various alcohol traits have shown many of the characteristics of human alcoholism. Furthermore, there appear to be correlation of genetic variation in brain neurochemistry and in inherited drinking behavior in these animals, thus providing additional evidence of a genetic influence in human drinking behavior.

Recent studies have demonstrated the interaction of genetic and environmental factors in the development of alcoholism. As a result of these studies, two subtypes of alcoholism have been identified. The more common type (Type 1) occurs in both men and women and the age of onset is usually above age 25. Type 1 alcoholism is associated with anxious personality traits and rapid development of tolerance and dependence on the anti-anxiety effects of alcohol. This leads to loss of control, difficulty terminating binges once they start and organ damage following prolonged drinking. In this subtype, environmental as well as genetic factors are involved. The second subtype (Type 2) is male-limited and typically has an early onset, before age 25. This subtype is associated with risk-taking and anti-social personalities and persistent seeking of alcohol for its euphoriant effects. Genetic factors appear to be far more important than environmental factors in the onset of this subtype.

A number of biological markers have been identified in population and family studies of alcoholics, which may prove useful for identifying individuals at high risk for alcoholism. Some potentially useful biological markers of alcoholism are described below:

Studies of young sons of alcoholic fathers and matched controls have revealed significant differences in brain electrical activity between the two groups. Earlier studies using resting

state electroencephalographic (EEG) recordings demonstrated more high-frequency activity (fast EEG) among sons of alcoholics. Reductions in amplitudes of evoked potential, particularly the P3 wave, were also observed in young boys (ages 7-13) who were never exposed to alcohol. Furthermore, young men with a family history of alcoholism reported less of a reaction to the effects of a challenge dose of alcohol than did subjects with no history of alcoholism. Blood concentrations of ACTH (adrenal corticotrophin hormone, released from the pituitary gland) and cortisol (an adrenal cortical hormone whose production is stimulated by ACTH) did not increase after drinking in the sons of alcoholics as much as in sons of nonalcoholics. These results suggested that the effect of alcohol consumption on blood ACTH and cortisol concentrations might be a useful biological marker to assess the risk of developing alcoholism. Another study reported that teenage boys who abused multiple drugs and had personality traits similar to those of Type 2 alcoholics also showed low monoamine oxidase (MAO) activity. Therefore, a low level of platelet MAO may be another marker of predisposition to alcoholism.

Dramatic advances in the mapping of the human genome have permitted scientists to investigate the genetic basis for complex diseases formerly considered to be multifactorial, that is, diseases resulting from the additive effects of many genes and environmental factors. The recent development of highly polymorphic DNA markers along with powerful new techniques in mathematical analysis and computer science make the prospect of "disentangling" the effect of a gene or genes for alcoholism a surmountable task. If a single gene strongly influences susceptibility to alcoholism, there is a 95 per cent probability that it will be linked with a known marker locus and will thus be discernible in a linkage study.

1990 - 1991 research:

In 1989 the Institute embarked on a major effort aimed at identifying the gene or genes that influence susceptibility to alcoholism by funding a large multi-disciplinary, multi-site collaborative study. This collaborative approach involves experts in a wide variety of scientific disciplines and allows environmental, psychological, and genetic factors to be studied simultaneously.

The research groups will collect data on alcoholics and their relatives, and a coordinating center has been set up to coordinate data collection and analysis. The research will focus on finding the genes associated with alcoholism and markers that will help in identifying individuals at risk for alcoholism. This collaborative study of alcoholics and their relatives will involve the collection of pedigrees of large families, the acquisition of immortalized lymphocytes or DNA for analysis of genetic markers and mapping studies, and investigations of the association of potential genetic and biological markers with the expression of the alcoholic phenotype within the families being

studied. The DNA from study subjects will be stored in a repository and will thus become a national resource that will eventually be made available to a broader range of the research community. Experts in molecular genetics, genetic epidemiology, mathematical statistics, psychiatry, and physiology will be involved in this complex undertaking.

In summary, due to recent advances in human genetics, the characterization of alcoholism is now being approached systematically. Previous human genetic studies have focused on whether alcoholism clustered in families and whether that clustering was due to genetic factors. The present studies are concerned with identifying specific genes that indicate a susceptibility to alcoholism. Studying the interaction of genes with environmental factors that increase or diminish the risk of alcoholism may well be the key to effective prevention or treatment of this major health problem.

HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Maternal and Child Health and Resources Development

GENETIC DISEASES

Title XI of the Public Health Service (PHS) Act formerly provided authority for the establishment of a national program to provide for basic and applied research, training, testing, counseling and information and education programs with respect to genetic diseases, including sickle cell anemia, Cooley's anemia, Tay-Sachs disease, cystic fibrosis dyautonomia, hemophilia, retinitis pigmentosa, Huntington's chorea and muscular dystrophy.

The Title XI authority was superseded by the Ominbus Budget Reconciliation Act of 1981, which modified Title C of the Social Security Act to provide for a Maternal and Child Health Service Block Grant, and included the Genetics Program as part of a 15% set-aside for discretionary Consolidated Federal Programs.

Genetic diseases are a significant health problem. In the United States, one child in every 150 to 200 live births or a total of 15,000 to 20,000 infants each year has a major genetic anomaly. A study in Baltimore, Maryland indicated that nearly one-third of hospitalized children had diseases that were "gene-influenced."

Currently 97 percent of newborn infants are receiving genetic screening, primarily for henylketonuria (PKU). This metabolic disorder which accounts for less than one percent of all genetic diseases causes severe mental retardation if untreated. In most instances of PKU and a few other genetic disorders, prompt diagnosis and treatment will prevent adverse effects. The reduction of genetic diseases is primarily dependent on early identification of carriers of genetic disease traits through screening, testing and appropriate genetic counseling. Amniocentesis is a procedure used to detect or rule out some genetic conditions in the unborn fetus. Provision of genetic counseling based on results of prenatal testing permits individuals to make an informed decision regarding the risks of having a child and/or prepares them for the care of an affected child.

Except for PKU and sickle cell disease screening, genetic screening and diagnostic and counseling services are generally less available to some segments of the population, especially those groups at high risk which are served by the Department of Health and Human Services (HHS) programs. Laboratory resources required for genetic testing are extremely limited. Since the inception of the Federal Genetics program, there has been a significant increase in the availability and linkage of genetic testing and counseling services to the rest of the health care delivery system.

Information on the incidence and prevalence of genetic disease varies considerably. For example, fairly well established figures are available for sickle cell anemia, cystic fibrosis and Tay-Sachs disease, while almost no reliable figure is available for retinitis pigmentosa; figures for diseases such as Huntington's chorea and muscular dystrophy vary widely. Similarly, the state of technological development in screening and testing also differs considerably for those diseases.

Identification of carriers of sickle cell anemia, Cooley's anemia and Tay-Sachs is possible through available screening tests, whereas identification of carriers for cystic firbrosis is still under study, and reports of available screening tests for carriers of hemophilia are sometimes not conclusive. The course of illness and prognosis also varies from Tay-Sachs disease, which is fatal in the first few years of life, to Huntington's chorea, which generally becomes manifest only in the fourth decade of life, although earlier onset is known to have occurred.

The major Genetic Diseases program in existence through Fiscal Year (FY) 1988 were the following:

Grant Programs for the Development and Operation of Statewide Genetic Diseases Systems - These projects continued development and implementation of Statewide or regional systems of genetic care. All projects coordinated their activities with existing health care delivery systems and especially with the Maternal and Child Health programs supported under Title V of the Social Security Act.

Sickle Cell - Multi-State programs for the education, screening and counseling of couples at risk for having an infant with Sickle Cell Disease or other hemoglobinopathy were continued. These projects stress cooperation between Sickle Cell clinics and heretofore unrelated tertiary Sickle Cell centers. Other projects demonstrate the value of newborn screening for hemoglobinopathies as a means of initiating early intensive, comprehensive care and preventing morbidity and mortality.

Genetic Networks - These projects are for the development and implementation of coordinated multi-State genetic services networks for defined geographic areas in order to provide better quality of care to the target population by sharing expertise and resources and providing more efficient means of access and service delivery.

Information and Education Services - The expansion of the National Clearinghouse for Human Genetic Disease and the National Center for Education in Maternal and Child Health has resulted in a much broader-based resource with improved access and dissemination of information related to all areas of Maternal and Child Health to State and local programs, private agencies and the public.

Interagency Agreements - Interagency agreements supported unique contributions from other HHS constituent agencies, such as the Center for Disease Control, for laboratory quality control through proficiency testing and standardization for PKU and congenital hypothroidism.

New HGB Screening Activities - Work continued from previous awards which established a new program focusing on hemoglobinopathies as required by the FY 1986 Omnibus Budget Reconciliation Act amendments to Title V of the Social Security Act.

PUBLIC HEALTH SERVICE AND GOVERNMENT-WIDE
HOMELESS
Budget Authority/Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
HHS					
ADAMHA	$52,198,000	$17,956,000	$49,095,000	$78,532,000	$76,069,000
HRSA	0	130,840,000	14,820,000	45,552,000	33,667,000
FSA	36,800,000	19,148,000	18,918,000	20,939,000	42,000,000
HDS	23,250,000	26,089,000	41,923,000	73,452,000	53,452,000
Total HHS	112,248,000	194,033,000	124,756,000	218,475,000	205,188,000
HUD	195,000,000	72,300,000	171,500,000	284,000,000	461,600,000
FEMA	125,000,000	114,000,000	126,000,000	130,100,000	125,000,000
DOL	0	9,600,000	9,400,000	11,300,000	13,000,000
DOEd	11,500,000	12,000,000	11,900,000	17,300,000	17,500,000
USDA	0	61,000,000	117,000,000	109,000,000	102,000,000
DOD	2,200,000	2,300,000	2,800,000	3,000,000	3,100,000
VA	25,000,000	13,000,000	23,700,000	30,000,000	30,000,000
Interagency Council	(200,000)	800,000	1,100,000	1,100,000	1,200,000
Total Homeless	$470,948,000	$479,033,000	$588,156,000	$804,275,000	$958,588,000

ALCOHOL, DRUG ABUSE AND MENTAL HEALTH ADMINISTRATION

National Institute of Mental Health

HOMELESS

HOMELESSNESS AND MENTAL ILLNESS

Perhaps no group of disabled people in the United States is as impoverished and poorly served as the homeless mentally ill population. All too often, homeless mentally ill persons are disenfranchised from their families, service providers, and communities. They are frequently excluded from programs designed to serve the general homeless population; they also have been screened out from receiving services designed for the long-term severely mentally ill. While homeless mentally ill individuals share characteristics and needs with the homeless population generally, the fact that they are mentally ill sets them apart and demands special approaches to ending their homelessness.

In March of 1989, the NIMH Director established a new Office of Programs for the Homeless Mentally Ill (OPHMI) within the Office of the Director. The Office provides leadership and coordination of an expanded Institute-wide effort to improve the care and treatment of mentally ill individuals who are homeless or at risk of becoming homeless. To assist the Office in these efforts, an NIMH Working Group on the Homeless was established comprised of representatives from each of the four NIMH research divisions. Because the needs of the homeless population are multiple and diverse, no single agency at any level of government can address the needs of this group alone. Therefore, the Office also works closely with the Federal Interagency Council on the Homeless, providing it with expertise on the mental health aspects of homelessness.

Since 1982, the National Institute of Mental Health (NIMH) has provided leadership in identifying the mental health, housing, and support needs of homeless mentally ill persons and in assisting States and localities in addressing those needs. This leadership takes the form of research, research demonstration, program evaluation and technical assistance activities designed to expand the boundaries of what is known about the homeless population; what is known about preventing homelessness among the mentally ill; and what is known about treating and re-housing those who are already homeless. Through such activities, NIMH is building a research base to guide the development of effective services and treatments for the homeless mentally ill.

Between 1982 and 1986, NIMH awarded 10 investigator-initiated research grants focused on the homeless mentally ill population. These studies, the first to provide an understanding of the relationship between homelessness and mental illness, were designed to assess the demographics, mental health status, and service needs of homeless individuals. A recently published synthesis of these

studies indicates that approximately one third of the homeless single adult population suffers from serious and disabling mental illnesses such as schizophrenia and manic-depressive disorder. Major findings of that report include: (1) the homeless mentally ill population has multiple needs (e.g., between 35-40 percent of this group also have a substance abuse problem); (2) many mentally ill homeless have had involvements with the criminal justice system, generally attributable more to their homelessness than anti-social or criminal behavior; (3) many homeless mentally ill persons have never received mental health treatment, and many homeless mentally ill persons formerly in treatment are no longer disabled by mental illness; (4) the mentally ill are over-represented among the homeless residing on streets as opposed to shelters and have more extensive needs in the aggregate than shelter users; and (5) a significant proportion of the population is interested in receiving help, but their perceptions of their own service needs often differ from the perceptions of service providers.

SCOPE OF THE PROBLEM

As the numbers of homeless individuals across the country have grown in recent years, the presence of a significant subgroup of mentally ill individuals among them has been an increasing source of professional and lay concern. NIMH service demonstration announcements define the homeless mentally ill population as adults, age 18 years or older, who have long-term, severe, disabling mental illnesses, and no fixed place of residence (or who are at imminent risk of becoming homeless). In this context, severe mental illness is defined as a serious and persistent mental or emotional disorder (e.g., schizophrenia, severe depression, manic-depressive disorder) that disrupts functional capacities for such primary aspects of daily life as self-care, interpersonal relationships, and work or school.

However, delineating the boundaries and size of the homeless mentally ill population is no simple task. Operational definitions of "homelessness" vary tremendously from study to study, encompassing a range of variables including lack of shelter, income, or social support. Given these definitional problems, it is difficult to precisely gauge the scope of the problem. For many years, the two most frequently cited estimates of the number of homeless persons in this nation have been 250,000-350,000 and 3 million. The first figure is the lowest estimated daily count of homeless persons used by the U.S. Department of Housing and Urban Development in its May 1984 national report on homelessness. The second figure is an estimate, extrapolated from disparate local studies, that approximately 1% of the population lacks shelter annually. Two recent studies have offered additional estimates of the total homeless population. The National Alliance to End Homelessness (1988) has estimated that, on any given night, the homeless number 735,000 while The Urban Institute, in a study funded by the Agriculture Department's Food and Nutrition Service,

concluded that the number of homeless people is between 567,000 and 600,000.

A recent General Accounting Office (GAO) Report (1988) reviewed 27 national, State, and local studies. The report acknowledges that there are no sound national estimates of the homeless or homeless mentally ill population and describes some of the particular problems in measuring the size of the latter group. As part of its 1990 census, the U.S. Department of Commerce's Bureau of the Census will count persons residing in public and private emergency shelters, persons in open locations on the streets or other places not intended for habitation and "doubled-up" families in an attempt to offer a more definitive estimate of the number of homeless persons in the United States. Although no specific information will be collected on the mental health status of homeless persons, the census data will provide mental health researchers with a sampling frame that can guide future research.

PROGRAM ACTIVITIES ON THE HOMELESS MENTALLY ILL

NIMH RESEARCH EFFORTS

In December 1988, NIMH issued a new research announcement, "Research and Research Demonstrations on Homeless Severely Mentally Ill Adults and Homeless Families with Children Who Are at Risk of Severe Emotional Disturbance". The announcement encourages investigator-initiated epidemiological, services, and service systems research on both homeless mentally ill adults and homeless families with children who are at risk of severe emotional disturbance.

Research on homelessness and mental illness has been quite limited by the myriad of methodological problems involved in the conduct of research on this topic. To begin to address this problem, in February 1989, NIMH sponsored a research development workshop; approximately 150 researchers were invited to participate in workshops and individual consultations designed to stimulate their interest in this patient population and to refine their research skills.

As a result of the workshop, 38 applications were submitted by the first deadline in April 1989 and 10 grant awards, totalling approximately $3.1 million, were made late in FY 1989. The duration of the projects funded ranges from three to five years. A number of the projects are longitudinal in nature, examining factors that lead mentally ill individuals to become homeless and interventions that can help them become housed.

Each of the grants is administered in one of the four NIMH research divisions. The Office of Programs for the Homeless Mentally Ill assists in providing technical assistance to potential grant applicants and in disseminating research findings to a broad audience of service providers, policy makers, and other

researchers. Descriptions of the seven research projects and three research demonstrations are as follows:

- **The Course of Homelessness Among the Seriously Mentally Ill (Audrey M. Burnam, Ph.D., RAND Corporation)** will examine the association between pre-homeless factors and homeless experiences among 1,500 homeless individuals with and without serious mental illness. A two-year panel study of a subset of 480 currently homeless persons will examine the course of homelessness among those with or without serious mental illness in two sites in Los Angeles County and will identify factors that predict exit from, and reentry into, homelessness.

- **Older Homeless Women (Carl I. Cohen, Ph.D., State University of New York Health Science Center at Brooklyn)** will work to develop an understanding of a sample of New York, homeless women over the age of 50. Investigators will describe the demographic, physical, psychiatric, psychological, and social characteristics of older homeless women and will contrast the findings with other subsets of homeless and general populations. The researchers will explore the pathways that lead to homelessness, examine informal social relationships and coping styles of older homeless women, determine the priorities and needs of service providers with respect to this group, and develop a theoretical model of adaptation to homelessness.

- **Women and Children in the Continuum of Residential Stability (Pamela J. Fisher, Ph.D., Johns Hopkins University)** will provide data on the social, health, and mental health characteristics of homeless women, their psychiatric disorders, and their capacity to care for their children. The study will also provide information on the development and emotional state of the children of these women. Investigators will study women and children along a continuum of residential stability ranging from long-term homelessness to stable domicile, comparing social and health characteristics of mentally ill women, women whose children are placed with other care-givers and women who are caring for their dependent children. Children being cared for in these various settings will also be compared.

- **Attitudes Toward the Homeless Mentally Ill (Bruce G. Link, Ph.D., Columbia University)** will conduct a national telephone survey of the general public's knowledge, attitudes, and beliefs about homeless and mentally ill homeless individuals. The goal of this survey is to fill important gaps in our knowledge of public opinion regarding the homeless such as which public conceptions are inaccurate or detrimental to the homeless, what policy interventions are most likely to be supported, and where educational programs to alter public conceptions might be fruitfully implemented.

- **Mental Illness Service Use and Homeless Careers (Marjorie J. Robertson, Ph.D., Alcohol Research Group)** is a longitudinal study designed to document the course of homelessness among adults with severe mental illness in Alameda County, California. Researchers will document the transition from homelessness to becoming housed and the vulnerability to subsequent homelessness among mentally ill and other homeless adults, and will assess how various mental health and service utilization factors affect this transition. They will also evaluate the degree to which sustained homelessness may affect functional status, and in turn, patterns of homelessness among mentally ill and other homeless adults.

- **Domestic Violence as a Risk Factor for Homelessness Among Women (Leonard Saxe, Ph.D., Boston University)** is a small study in which the investigator will compare two groups of 50 women each, one homeless and the other housed, to evaluate whether a history of domestic violence (child physical or sexual abuse and spouse abuse) is a risk factor for homelessness.

- **Rural Homelessness in Ohio: A Five-Year Study (Beverly G. Toomey, Ph.D.,Ohio State University)** will replicate the non-urban component of a 1984-85 NIMH supported study, "Homelessness in Ohio: A Study of People in Need," which documented the prevalence of mental illness and the service needs found in the homeless population. The current study will identify changes over five years in the size and characteristics of the rural homeless population, develop additional knowledge about the causes of rural homelessness, estimate the prevalence of mental illness among the rural homeless in Ohio, and study service access and utilization among the homeless mentally ill population.

- **Assertive Case Management for Dually Diagnosed Clients (Robert Drake, M.D., New Hampshire Department of Health and Human Services)** will develop an effective case management intervention for individuals with a dual diagnosis of substance abuse and chronic mental illness and will clarify pathways into and out of homelessness among a subset of the study population. The investigators will develop and maintain a continuous treatment team in Manchester, New Hampshire, that will combine the principles of assertive case management with integrated treatment for substance abuse and mental illness. They will compare this effort with standard case management in community support programs.

- **Cost Effectiveness of Case Management for the Homeless (Gary Morse, Ph.D., Malcolm Bliss Mental Health Center)** will test the effectiveness of different case management models by randomly assigning homeless mentally ill clients to one of three programs - an intensive case management program that incorporates community workers as members, a case management program staffed entirely by professionals, and a standard

"service broker" case management program. The investigators will examine variables that mediate client outcomes over an 18-month follow-up and will evaluate the cost effectiveness of each of the three treatment programs.

- **Case Management for Jailed Homeless Chronically Mentally Ill: Two Models (Phyllis Solomon, Ph.D., Hahnemann University)** will test the relative effectiveness of two models of intensive case management for homeless severely mentally ill individuals who are being released from the Philadelphia County prison system. Two hundred individuals will be randomly assigned to a forensic community treatment team, a prevailing specialized individual case management intervention, or a minimal treatment group.

The NIMH homeless research portfolio also includes three research grants begun before FY 1989. The FY 1989 grant awards for these projects total $468,520. One study has collected extensive data on urban homeless persons interviewed on the streets of Baltimore and in city missions, shelters, jails, and parks. It has found that more than a third of the homeless men and nearly half the homeless women have a diagnosis of major mental illness. Homeless persons in the city jail were found to have the most pathology and the highest rates of prior hospitalization. The data indicate a high level of disaffiliation of the homeless population and their heavy involvement in substance abuse.

Another study is evaluating the efficacy, strengths, and weaknesses of the St. Louis, NIMH-sponsored, Community Support Program (CSP) for the homeless mentally ill. The research is evaluating clients in three treatment conditions: a case manager/advocate program (the CSP intervention), an existing daytime drop-in center, and a traditional outpatient therapy program. Preliminary data suggest that clients in the CSP have lower attrition, are more satisfied with their care and are housed more days than the day treatment clients.

A third study is aimed at determining the causes of homelessness among schizophrenic young adult males. Through a case-control design, the researcher is comparing 100 homeless shelter users and 100 other schizophrenic men in psychiatric aftercare in New York City on several dimensions including family disorganization in childhood, caretaker burden, and prior mental health service use.

In addition to research grants, a relevant Research Scientist Award has been made to Richard Tessler of the University of Massachusetts at Amherst. His five-year award supports added effort in studies of continuity of care and family burden and his research on the homeless mentally ill.

10

SERVICES DEVELOPMENT EFFORTS

In 1984, Congress amended the Public Health Service Act to authorize funding of mental health services demonstration projects for the planning, coordination, and improvement of community-based services for persons with severe, long-term, disabling mental illnesses. Under this authority, between 1985 and 1987, the NIMH Community Support Program (CSP) provided funding support for 20 local demonstration projects focused on the homeless mentally ill population. The amount of Federal grant support was limited to approximately $125,000 per project, and the funds were used to demonstrate discrete service components.

The passage of the Stewart B. McKinney Homeless Assistance Act (Public Law 100-77) has provided an unprecedented opportunity for the Federal government to expand both its research and service demonstration efforts on behalf of the homeless mentally ill. The Act authorizes a competitive grant program entitled, "Community Mental Health Services Demonstration Program for Homeless Individuals who are Chronically Mentally Ill." Twelve two-year demonstration projects were funded with a FY 1987 appropriation of $9.3 million. Nine projects are designed to implement and evaluate comprehensive community based services for homeless adults with mental illnesses (Florida, Illinois, Michigan, New York, Ohio, Oregon, South Carolina, Tennessee, and Virginia); three smaller projects are designed to test innovative, targeted approaches to serving severely emotionally disturbed homeless children and adolescents (District of Columbia, Maine and Vermont). Eight of the projects were competitively renewed for a third year with a FY 1989 appropriation of $4.6 million.

Each of the projects designed for homeless mentally ill adults is required to provide certain mental health and related services. These include outreach services in nontraditional settings (e.g., shelters, drop-in centers), intensive, long-term case management, mental health treatment, staffing and operation of supportive living programs, and management and administrative activities that are designed to link together services into a comprehensive system of care.

As of the spring of 1989, the nine adult demonstration projects had contact with 2,468 homeless individuals, assessed the mental health status of 1,381 homeless individuals, and provided direct services to approximately 865 homeless mentally ill people. The three projects for homeless children and adolescents had served approximately 500 children and youth who were either emotionally disturbed or at high risk of emotional disturbance.

It is likely that over the next decade, there will be a continued expansion in State and local services initiatives concerned with the homeless mentally ill population. However, as the mental health community expands its efforts, it is apparent that initiatives must be guided by the ongoing experimentation and evaluation. Therefore, a fundamental component of the NIMH demonstration program is its multi-phase evaluation and research strategy.

In the area of evaluation, an incremental series of studies is planned. The first effort, recently completed under contract with Research Triangle Institute, was a study to design a national evaluation of the implementation of the demonstration program and to assess the feasibility of conducting an effectiveness evaluation. As part of this initial study, an examination of the underlying logic of the program and the individual projects was conducted following the framework of an evaluation assessment. The actual national implementation evaluation, which began in the Fall of 1989, will yield cross-site, uniform data on both the implementation and effectiveness of the demonstration projects. The information from this effort will include data on the populations served, the nature of the specific services and service systems implemented, the client and system level outcomes of the projects, and the conditions that both facilitate and thwart project success. The national evaluation will be coordinated with and build upon each of the required individual project evaluation efforts and will establish a foundation for future studies of the effectiveness and impact of State and local initiatives.

In FY 1990, NIMH intends to use its Section 612 McKinney funds to solicit applications for research demonstration projects that test the effectiveness of certain services for the mentally ill homeless. Specifically, the projects will assess comprehensive mental health services and a range of housing alternatives provided the seriously mentally ill among the homeless. These projects will involve collaboration between the department of Housing and Urban Development (HUD) and the Department of Health and Human Services (HHS). Between five and ten new awards will be made in September 1990.

TECHNICAL ASSISTANCE EFFORTS

NIMH also has initiated a broad array of knowledge dissemination and technical assistance projects to assist its grantees and other service providers in meeting the needs of the population. The most recent and, perhaps, ambitious of these efforts has been the establishment of a National Resource Center on Homelessness and Mental Illness (operated by Policy Research Associates, Inc. in Delmar, New York). The mission of the Center (which was first funded in July, 1988) is to improve service delivery to homeless mentally ill persons by assisting other Federal, State, and local programs (both public and private) through the collection, development, synthesis, and dissemination of information on effective approaches to serving the population. Several of the primary activities of the three-year contract to the Center include: a quarterly newsletter that features news on the latest developments in programs, training, research, and legislation; a clearinghouse with an up-to-date and comprehensive bibliographic database of information on homelessness and mental illness; developing expert papers on service delivery issues that are not adequately addressed in the current literature; and sponsoring

workshops on substantive topics of interest to service providers. Accessibility to the Center has been enhanced by the provision of a toll-free telephone number. In its first 12 months of operation, the Center filled 1,532 requests for information. The average turnaround time for any request for information was less than one day.

NIMH has also supported numerous meetings and publications to provide information to service providers working with the homeless mentally ill population. A sample of the topics covered include:

- "Enhancing Mental Health Services for Homeless Persons: State Proposals under the Mental health Services for the Homeless Block Grant Program"
- "A Synthesis of NIMH-Funded Research Concerning Persons who are Homeless and Mentally Ill"
- "Research Methodologies Concerning Homeless Persons with Serious Mental Illness and/or Substance Abuse Disorders"
- "Service Needs of Homeless and Homeless Mentally Ill Minority Persons"
- "Engaging Homeless Persons with Mental Illnesses into Treatment"

One of the key features of NIMH's efforts on behalf of the homeless mentally ill population has been its close collaboration with other Federal agencies. In particular, NIMH has worked closely with the National Institute of Alcohol Abuse and Alcoholism (NIAAA), the National Institute of Drug Abuse (NIDA), and the Health Resources and Services Administration (HRSA) in coordinating research and technical assistance initiatives concerning the homeless population. The Department of Housing and Urban Development (HUD) and HHS are developing a memorandum of understanding to encourage closer collaboration between the two departments; FY 1990 should afford NIMH unique opportunities to influence Federal housing policy for the mentally disabled.

National Institute on Alcohol Abuse and Alcoholism

HOMELESSNESS

Research results of the last 10 years on the epidemiology of homelessness in the United States have converged on one significant finding: a large proportion of homeless persons suffer from alcohol and other drug problems. No fewer than 35 percent of homeless persons have alcohol problems; an estimated additional 10 percent abuse other drugs. Moreover, problems of homelessness, alcohol and other drug abuse typically coexist with other health and mental health problems.

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) has responded to the problem of homelessness and alcohol and other drug problems through a number of research efforts. These include a large scale, multi-site research demonstration program and several studies focused on the magnitude and distribution of alcohol and other drug problems among homeless persons. These research efforts are described in more detail below:

Research Demonstration Program

The Community Demonstration Grant Projects for Alcohol and Other Drug Abuse Treatment of Homeless Individuals are funded under Section 613 of the Stewart B. McKinney Homeless Assistance Act (P.L. 100-77). In May 1988, the NIAAA (in consultation with the National Institute on Drug Abuse (NIDA)) funded nine community-based demonstration projects specifically targeted on homeless persons with alcohol and other drug problems. A total of $9.2 million was appropriated for a two-year period. An additional $4.5 million was made available for a third year competitive renewal of the original demonstration projects. Most of the projects were funded for a third year.

The mission of the NIAAA/NIDA research demonstration program is to provide and evaluate a variety of approaches to community-based alcohol and/or other drug abuse treatment for individuals with alcohol and other drug-related problems who are homeless. The primary goals of the program are to:

- reduce levels of alcohol and other drug abuse in persons who find themselves homeless;
- improve residential status by increasing access to emergency shelter and housing (including alcohol-free living environments);
- increase cooperation and formal linkages among alcohol treatment, and other human service agencies;
- improve economic status of target population by assisting vocational training and finding employment; and,

- improve the quality of life of the target population.

Grant awards were made on a competitive basis to nine programs in the following cities: Anchorage, Boston, Los Angeles, Louisville, Minneapolis, Oakland, Philadelphia (two programs), and New York. These projects responded to the goals of the demonstration with an array of approaches to providing alcohol and other drug treatment to persons with these problems. Among the service components included in these projects are:

- outreach and engagement services which seek out homeless persons in their natural environment in an attempt to engage them in formal services;
- establishment of shelters, drop-in centers, and sobering stations that serve as a first point-of-contact with the human service system;
- alcohol treatment recovery services such as detoxification, individual and group counseling, and self-help groups;
- case management services which include outreach, assessment and evaluation, service planning, advocacy, benefits acquisition, service linkage and service monitoring;
- transitional housing and alcohol-free living centers; and,
- vocational training.

These services are provided by the grantees to a variety of subpopulations--namely, chronic public inebriants, women with children, persons who are experiencing both mental illness and alcohol and other drug problems, and, in two projects, Native Americans.

Evaluation of project effectiveness has been given a high priority in the NIAAA demonstration projects. Twenty-five percent of each grant award has been devoted to evaluation research efforts. Grantees are required to conduct client-level process evaluations and outcome evaluations of their programs where possible. The evaluation designs currently being implemented will assess client outcome using a variety of experimental and quasi-experimental designs and will be measured using standardized assessment instruments (e.g., the Addiction Severity Index) as well as qualitative data gathered from staff, administrators and clients. Several projects are evaluating program impact on the network of services for homeless persons. Grantees are also required to participate in a national evaluation of the services demonstration project. The national evaluation effort will have three components: systematic case studies, site-level process evaluation, and a cross-site analysis of client outcome.

Research Studies

NIAAA has funded several research grants focused on the homeless that complement the research demonstration program. For example, NIAAA sponsored a survey of homeless youth residing in shelters and on the streets in Los Angeles. Nearly one-half of the respondents had a diagnosis of alcohol and other drug abuse dependence. In a second project, the nature of alcohol and other drug problems among a national sample of homeless persons who used the Robert Wood Johnson (RWJ) Health Care for the Homeless clinics is being analyzed. (The RWJ project is the first opportunity to gather data on the homeless on a national scale.) A third project, funded in FY 1989, is investigating the effectiveness of intensive case management services for persons suffering from alcohol abuse and mental illness. In a fourth project, NIAAA has funded a literature review of studies that estimate the prevalence of alcohol and other drugs among the homeless. The purpose of this literature review is to develop a more precise estimate of the prevalence of alcohol and other drug abuse among the homeless, and develop a better understanding of the sources of bias unique to estimating prevalence statistics with this population. Finally, NIAAA sponsored a research conference in February 1989 specifically devoted to homelessness, alcohol and other drugs. This conference brought together researchers from around the nation to present their findings and identify issues for future research on homeless persons with alcohol and other drug problems.

Plans for FY 1990

In FY 1990, NIAAA and NIDA will support a second generation of research demonstration grants. The focus of these grants will be on assessing the efficacy of a variety of client-centered interventions that focus on providing individual services to homeless persons with alcohol and other drug problems. Grant funds will be used to assess a variety of treatment interventions including outreach, sobering, detoxification, shelter, recovery and treatment, case management, and alcohol and drug-free residences. The evaluation of combinations of these service components will also be encouraged. These grants will be awarded for a three year period with annual awards being made subject to continued availability of funds and progress achieved.

As with the FY 1988 research demonstration program, the FY 1990 demonstration program will place a great deal of emphasis on evaluation of treatment approaches and patient outcome. Projects will be encouraged to use the strongest possible research designs (at minimum, quasi-experimental designs) to assess client outcome. NIAAA will also encourage multi-site evaluations of interventions proposed by applicants. Individual projects will evaluate implementation and outcome questions such as: What are the characteristics of the individuals who are served? What services do they receive? Do the services make a difference in

terms of providing help with problems of homelessness and alcohol and other drug use?

Grantees also will be required to participate in a national evaluation to be conducted in cooperation with NIAAA. The national evaluation will include standardized measures of client demographic characteristics, service utilization, alcohol consumption (including physiological measures), residential stability and employment status. In addition, this information will be used to determine the most effective treatment approaches for various client groups.

Up to 18 awards are planned for September, 1990.

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HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Health Care Delivery and Assistance

HEALTH CARE FOR THE HOMELESS

Under the Stewart B. Mckinney Homeless Assistance Act of 1987, the Bureau made awards to community-based organizations and coalitions to provide primary health care, substance abuse, mental health, and case management services to homeless individuals. As a means of improving access to community services, all Health Care for the Homeless Programs (HCHP) have developed linkages , i.e., community coalitions(where none existed) which have included both public and voluntary agencies and programs that offer such services as meals, shelter, social services, employment training, and job placement.

The 109 HCHP projects represent both rural communities and large metropolitan areas and include organizations such as local Health Departments, Robert Wood Johnson/PEW foundation demonstration projects, community and migrant health centers, and substance abuse and mental health programs. Projects are supported in 41 States, the District of Columbia, and the Commonwealth of Puerto Rico. It is estimated that the primary health and substance abuse services provided by the 109 HCHPs will benefit approximately 400,000 individuals during 1990. Each of these has been actively involved in developing local coalitions composed of health care providers and social services agencies in an effort to maximize community resources for the provision of related services such as food and clothing, shelter, employment training, and job placement.

HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Health Professions

Homeless Health Initiatives

Three Physician Assistant Training program grantees provide educational experiences for 45 students in dealing with the physical and mental health needs of the homeless population.

The health care needs of the homeless are included in the residency training offered by one Family Medicine Graduate Training program, which is expected to impact 18 individuals.

1.

FAMILY SUPPORT ADMINISTRATION

Homeless Assistance

The McKinney Act, as amended, provides funds under the Emergency Community Services Homeless Grant Program (EHP) to assist families and individuals who are homeless or are about to become homeless. The EHP funds may be used to: (1) expand comprehensive services to homeless individuals to provide follow-up and long term services to enable the homeless to move out of poverty; (2) provide assistance in meeting social and maintenance services for homeless individuals; (3) promote private sector and other assistance to the homeless; and (4) after October 1, 1988, use up to 25% of funds annually to provide assistance under certain conditions to an individual who has received a notice of foreclosure, eviction, or termination of utility services, in order to prevent them from becoming homeless.

EHP funds provide services for homeless families and individuals through a national network of local anti-poverty agencies. These resources, and mobilize millions of hours of volunteer services. The impact of these funds can best be understood by looking at the range of services and activities provided to homeless families, children, and single men and women. The EHP program is very flexible and can be used for almost any goods or services that help the homeless, including food, shelter, counselling, case management, transportation, medical care, and day care.

EHP funds awarded to States, territories, and federally-recognized Indian tribes are being used to provide the following services:

- emergency and temporary shelters
- food provided through pantries and soup kitchens
- medical and/or transportation assistance
- counselling on drug abuse, domestic violence and runaways
- case management, or referral to other agencies, groups and/or services
- clothing, blankets and emergency services
- housing assistance
- employment assistance and hiring incentives to private sector organizations
- outreach assessment and counselling
- fund solicitation from companies and corporations
- promotion of fund raising efforts
- day care

OFFICE OF HUMAN DEVELOPMENT SERVICES

Homeless

The purpose of the Runaway and Homeless Youth Program is to provide financial assistance to establish or strengthen community-based centers designed to address the needs of runaways and homeless youth and their families. Funding for fiscal year 1990 will support approximately 355 runaway and homeless youth shelters as well as the national toll-free runaway youth hotline. In fiscal year 1987, nearly 23,000 (or approximately one-third) of the youth seeking over night services identified themselves as being homeless.

The Transitional Living Program for Homeless Youth, funded for the first time in fiscal year 1990, addresses the shelter and service needs of homeless youth through financial support and technical assistance to public and private non-profit entities. Grants will be used to (1) develop or strengthen community-based programs which assist homeless youth in making a smooth transition to a productive adulthood and social self-sufficiency and (2) provide technical assistance to transitional living grantees to enhance their capacity to acquire and maintain resources and service linkages in their local communities to benefit program participants.

The Drug Education and Prevention Program for Runaway and Homeless Youth authorizes grants to public and private non-profit agencies, organizations and institutions for research, demonstration and service projects, but requires the Secretary to give priority to agencies that have experience in providing services to runaway and homeless youth. Grants under this program support counseling, community education, training and information, research, and other activities to improve the availability and coordination of local services related to drug abuse for runaway and homeless youth.

During fiscal year 1989, competitive grant awards were made to 104 agencies and organizations representing 35 States and the District of Columbia to improve or expand existing services; develop networking efforts in rural and other areas with minimal services; develop innovative model programs; and serve Native American youth. In addition, a contract was awarded to develop a prototype drug education training program and to provide technical assistance to runaway and homeless youth service providers.

In fiscal years 1990 and 1991, $14,801,000 will support the continuation of service and demonstration grants in the areas of comprehensive service delivery and resource development for runaway and homeless youth and their families and for training programs for youth service providers and of contracts for research, technical assistance, monitoring and evaluation of grantee activities.

In addition, States may use Social Services Block Grant (SSBG) funds for services to the homeless. However, States are not required to report the amount of funds used for such services.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
SOCIAL SECURITY ADMINISTRATION

Homeless

Retirement and Survivors Insurance

Social Security Retirement and Survivors Insurance (RSI) benefits are payable directly to (1) retirees at age 62; (2) dependents of retirees (i.e., wives, husbands, children age 18 or younger, and unmarried adult children disabled before age 22); and (3) survivors (i.e., widows/widowers at age 60, or at age 50 if disabled, children age 18 and younger, and unmarried adult children disabled before age 22). These benefits provide a minimum level of income support that may help prevent some elderly from becoming homeless.

Disability Insurance

The Social Security Disability Insurance (DI) program pays monthly disability benefits to workers under age 65 and their families. Disabled workers must have worked long enough and recently enough under Social Security to be insured under this program. The work requirement varies depending on the age of the worker. Under Social Security, persons are considered disabled if they have a severe physical or mental condition that prevents them from working and that is expected to last (or has lasted) for at least 12 months or is expected to result in death.

Disability Insurance payments can start at the beginning of the sixth full month of a disability. Once payments start, they will continue as long as the person remains disabled and unable to perform substantial gainful work. Cases are reviewed periodically to make sure that the person's disability has persisted. DI claims can be filed with a request for up to 12 months' retroactivity. While some benefits may be received by disabled homeless individuals, there are no data on the extent of such payments.

Supplemental Security Income

The Supplemental Security Income (SSI) program makes monthly payments to people who are at least age 65 or disabled or blind and have little or no income and assets. Most States supplement the Federal SSI payments and provide Medicaid. Also, some people who are residents of public emergency shelters can now receive SSI payments for up to six months during any nine consecutive month period. Eligible persons who live in private shelters are unaffected by this six-month limit.

Outreach Activities

Under the direction of the central office, Social Security Administration (SSA) field offices have established various outreach activities and special procedures to meet the problems faced by the homeless in obtaining any Social Security or SSI benefits for which they are eligible. Some examples follow.

- Regional and local directories of services for the homeless have been published and distributed to shelters and local social service agencies.

- Local SSA managers and employees work closely with local shelters and advocates to help SSA serve the needs and protect the rights of the homeless by assuring representation in the claims process, providing representative payees where needed and working out check delivery problems.

- Contact stations have been established in shelters in many cities. In some locations special procedures have been established to expedite the decision-making process regarding disability claims. For example,

  -- in New York, State Human Resource Administration doctors perform on-site medical exams during the joint visit of SSA and State Disability Determination Services staff to shelters; and

  -- in Los Angeles, the county Department of Mental Health prepares psychosocial histories and carries out psychiatric evaluations for the homeless and then schedules them for SSA interviews (the county Department of Mental Health also represents the individual during the claims process, assuring that necessary medical information is provided).

- Local programs have been developed, in conjunction with other agencies, to actively seek out homeless people and maintain contact with them during the processing of SSI claims.

- Pre-release arrangements with local public medical and domiciliary care institutions enable SSA to identify potential homeless situations. Claims are taken from such patients before their release to provide some money to use for housing costs upon release. SSA will also complete a food stamp application at the same time as the SSI application in these cases.

- SSA is cooperating with the Robert Wood Johnson Foundation in two of its nine project sites for homeless and chronically mentally ill people. Local SSA field offices work with the foundation's network of medical facilities to improve outreach to homeless people. SSA is serving in an advisory role in the foundation's project for the chronically mentally ill and exploring ways to work with the grantees in nine selected cities.

SSA also works with several national organizations that serve as advocates for homeless people to provide materials and information to be disseminated to affiliates, professionals and consumers. Information from these organizations also has been valuable to SSA in forming policies and procedures.

Commissioner King has made outreach a high priority for the Agency. She has established a taskforce which has developed a strategy for identifying potentially eligible people including the homeless and helping them obtain SSI benefits.

The Agency is

- developing minimum standards of outreach action for field offices;

- designing training material on SSA's program for community organizations that serve the needy and homeless;

- developing cooperative approaches with community organizations that serve the needy and homeless by helping them apply for benefits.

In addition, SSA is preparing a series of "best practices" issuances that describe projects dealing with the homeless and other categories of hard-to-reach people that are working well in one setting and have potential for proving successful in another. These issuances should allow SSA offices and other service providers to give active consideration to practices that have already been proven in other areas.

SSA is also developing a videotape to assist service providers in understanding SSI eligibility requirements and the methods by which SSA processes claims.

Additionally, SSA is implementing a grant program, funded in FY 1990, to address barriers to participation in the SSI program. Homelessness is a barrier, along with related problems that the homeless frequently have such as mental illness. The grants will be used to fund organizations and State or local agencies to develop effective ways of overcoming such barriers.

HUNTINGTON'S DISEASE
Obligations

	1987	1988	1989	Estimate 1990	Estimate 199:
Public Health Service:					
National Institues of Health:					
National Institute of Neurological Disorders and Stroke.....	$24,038,000	$23,907,000	$29,612,000	$30,557,000	$31,154,000
National Institute on Aging.....	---	---	959,000	992,000	1,032,000
TOTAL, NIH.....	24,038,000	23,907,000	30,571,000	31,549,000	32,186,000

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Disorders and Stroke

HUNTINGTON'S DISEASE

Although the specific nature of the genetic defect that causes Huntington's disease (HD) is still unknown, scientists supported by the National Institute of Neurological Disorders and Stroke (NINDS) continue to make progress in finding the answer. Research advances have heightened hope for development of an effective therapy, and possibly for preventing its occurrence. At the same time, NINDS-funded research has been critical in identifying HD patients and persons at risk and in defining the characteristics of this frightful affliction.

About 25,000 people in the United States suffer from HD, which is marked by a progression of uncontrolled, abnormal body movements, behavioral changes, and inevitably death. An affected parent can pass HD along to his or her offspring, and each child of a parent with HD will have a 50 percent chance of inheriting the HD gene and developing the disease. At least 100,000 people live in fear that they may have inherited the abnormal gene. NINDS-supported scientists are working on the development of standard diagnostic and assessment criteria.

HD usually becomes evident between the ages of 35 and 45, but no age is exempt. The first signs may be subtle--clumsiness or irritability. Over 10 to 20 years the symptoms worsen, resulting in a slurring of speech, continuous uncontrollable movements, and mental breakdown. The symptoms result from selective degeneration of brain cells. The most affected parts of the brain are the caudate nucleus and the putamen, structures involved in movement coordination that are located deep in the brain's basal ganglia. The cerebral cortex, which controls thought, perception, and memory, is often affected.

Many of the recent advances in HD research have been made possible through rosters of affected families, which provide access to multiple generations of genetic and other research material. The Huntington's Disease Research Roster, maintained by NINDS grantee Dr. Michael Conneally at Indiana University in Indianapolis, includes 1,519 families of 85,701 individuals, of whom 8,738 have HD. Another important set of data includes the largest known HD family, one in Venezuela whose pedigree now numbers about 10,000.

Understanding HD Genetics

Much exciting HD research is under way at the genetic level, as scientists zero in on the tip of chromosome 4 where the HD gene is thought to lie. The process of isolating the responsible gene has been more arduous than expected, but scientists still

hope to find the gene and then determine the role of its protein product in HD in the relatively near future.

In each HD family, certain characteristic markers--segments of DNA--travel with the HD gene as it is passed from generation to generation, thus signaling the gene's presence even though it has not yet been isolated. Scientists have been using DNA linkage analysis--a technique based on the tendency of certain genes to be inherited in tandem--to map the chromosome by locating markers that are closer and closer to the critical zone thought to include the site of the gene. Since the first marker was discovered 7 years ago by NINDS grantee Dr. James Gusella of Massachusetts General Hospital in Boston, more than 40 of these signposts have been discovered.

A Genetic Basis for Early Onset?

Research has shown that individuals who manifest HD symptoms at a younger age usually inherit the gene from their fathers. And the younger the onset, the faster the progression of the disease. A team headed by Dr. Gusella has investigated the possibility that some protective factor in the mother's genes may act to delay onset of HD symptoms. Since genes for mitochondria (the energy-producing elements of cells) are inherited only from the mother, Dr. Gusella's group traced these genes through eight generations of the Venezuelan pedigree. They found the genes to be identical in both early and late onset cases, and therefore concluded that the mitochodrial genes do not play a part in determining onset age in HD. The search continues.

Predicting Risk

Through DNA linkage analysis, scientists can test at-risk individuals for the presence of the HD gene. The tests are considered 99 percent accurate if sufficient information on relatives is available. About a third of attempted tests have not been useful because of insufficient information on family members. Investigators continue to assess the psychological effects of both positive and negative test results.

In an 18-month trial overseen by NINDS grantee Dr. Richard Myers at Massachusetts General Hospital, 35 people were tested. Six were diagnosed with HD, 8 were probable gene carriers, and 11 were probable noncarriers. All continue to be monitored for long-term psychological effects of the test. One person has required psychiatric hospitalization and medication for depression as a result of the test. Dr. Myers, however, describes the testing process as basically nonthreatening when administered by people experienced in the psychological effects of genetics testing.

The Johns Hopkins University in Baltimore, Maryland, conducts a research program on presymptomatic testing under the leadership of NINDS grantee Dr. Jason Brandt. As of Fall 1988, 53 people had been tested. Nine tested positive for the markers and 29 tested negative. In fifteen cases, the risk could not be determined. The NINDS-supported Johns Hopkins scientists have found that group--rather than individual--educational sessions are effective in explaining the technical and psychological aspects of testing without significantly increasing anxiety of at-risk individuals. Based on the results of questionnaires, the researchers found that anxiety levels actually were lower at the time of testing than at the end of the preceding educational sessions.

Learning More About Symptoms

In investigations of cognitive effects, NINDS grantee Dr. Marshal Folstein and colleagues at The Johns Hopkins University found that HD does not specifically affect attention, vigilance, span of apprehension, or distractibility. However, their studies did confirm evidence of deficits in learning to follow patterns. In repeated trials with a computerized maze that had a predictable pattern, HD patients showed no improvement in performance.

Moving Toward Treatment

Scientists suspect that the neurotoxin quinolinic acid, which occurs naturally in the brains of humans, is a prime candidate for the damage-causing agent in HD. Investigators have also found that grafts of tissue from the neonatal rat brain's striatum (a part of the basal ganglia) can reduce quinolinic acid damage in adult rat brains. NINDS grantee Dr. Noel Tulipan at Vanderbilt University in Nashville, Tennessee has produced an extract of neonatal striatal cells which, when injected into the rat brain with quinolinic acid, confers protection from quinolinic-acid-induced damage similar to that seen in tissue grafts. Dr. Tulipan is now proceeding to isolate the putative factor responsible for the extract's protective effect.

At The Johns Hopkins University, a team headed by Dr. Marshal Folstein has been studying the cause of toxin-induced neuronal degeneration, which is suspected to be a mechanism at work in HD. The scientists have examined the effects of idebenone--an agent used to treat certain forms of dementia--against such damage, and have found the drug highly protective. Their data suggest that idebenone might be a useful preventive treatment for HD.

Finally, investigators report promising early results with a technique that eventually might lead to a treatment. Past research has shown that rat fetal striatal tissue, when implanted

in a chemically lesioned rat brain, takes on many characteristics of normal host cells. The transplanted tissue even restores circuitry to denervated areas. Based on these remarkable results, Dr. Gusella's team at Massachusetts General Hospital has proposed using the technique in more advanced animal species. Preliminary work suggests that even cross-species transplants have beneficial effects, at least in reducing spastic movement.

Brain Imaging Research

Brain imaging technologies continue to contribute significantly to the quest for more information about HD. CT scanning is being used by Dr. Marshal Folstein at The Johns Hopkins University to assess relationships between neuropsychological deficits and brain abnormalities in HD. His scans reveal significant correlations between atrophy of the brain's caudate nucleus and such symptoms as abnormal eye movement and degree of dementia. Involuntary movement, however, was not linked to an atrophied caudate.

Looking Ahead to the Huntington's Challenge

The continued quest for the HD gene will require new approaches. To that end, scientists are working to develop a strain of mice that carries and expresses the human HD gene and can serve as a model for study. In addition, investigators plan to compare chromosomes within rare families where HD suddenly appears and is passed on to offspring after several healthy generations. Also under study will be those extremely rare HD patients whose parents both contributed an HD gene. Such individuals may possess a critical clue not detectable in patients with an HD gene from only one parent. Meanwhile, scientists press on, using increasingly more effective genetic mapping and sequencing techniques in their search for the gene that causes this severe, eventually lethal disease.

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HYPERTENSION

Obligations

National Institutes of Health:	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
National Heart, Lung, and Blood Institute	$100,797,000	$96,416,000	$98,179,000	$98,500,000	$102,500,000
National Institute of Dental Research	---	---	255,000	256,000	265,000
National Institute of Neurological Disorders and Stroke	4,024,000	3,998,000	4,331,000	4,469,000	4,675,000
National Institute of Child Health and Human Development	2,544,000	3,773,000	6,168,000	6,400,000	6,800,000
National Institute of Environmental Health Sciences	107,000	111,000	115,000	119,000	124,000
National Institute on Aging	6,119,000	5,203,000	6,215,000	6,432,000	6,687,000
Division of Research Resources	10,052,000	5,823,000	6,650,000	6,078,000	6,844,000
National Center for Nursing Research	464,000	289,000	522,000	590,000	590,000
Office of the Director, NIH 1/	635,000	902,000	641,000	733,000	---
TOTAL, NIH	124,742,000	116,515,000	123,076,000	123,577,000	128,485,000

1/ Represents funds awarded through BIDs for the Research Centers and Minority Institutions program

NATIONAL INSTITUTES OF HEALTH

National Heart, Lung, and Blood Institute

HYPERTENSION

Hypertension, or high blood pressure, is considered a major risk factor for the most commonly encountered forms of heart and blood vessel diseases. It is the single most important contributing factor to the development of stroke, and it accelerates the development of atherosclerosis of the coronary and peripheral arteries. People with hypertension are therefore at greater risk of dying prematurely from stroke or heart attack, and they also are more likely to develop kidney disease.

About 58 million Americans, one-fourth of the U.S. population, have high blood pressure. The prevalence is even higher among the elderly and among blacks. More than six in every 10 older Americans have hypertension, and more than four in every 10 black Americans have the disorder. By treating their hypertension, many of these individuals can reduce their risk of illness and death from heart and blood vessel diseases.

During the past 20 years, changes have occurred in the control of hypertension. The public is more knowledgeable about hypertension, more likely to visit a physician for hypertension, and more likely to follow medical advice. During this same period, there has been a 57 percent decline in the national age-adjusted stroke mortality rate, as well as a 46 percent decline in mortality from coronary artery disease. It is likely that increasing attention to hypertension management is one of the major factors in these declines.

Nevertheless, heart and blood vessel diseases remain the leading cause of death in the United States, and hypertension remains an important health problem. The areas of the world where hypertension is most prevalent are culturally more heterogeneous and share certain environmental characteristics (for example, excess sodium ingestion, sedentary life-style, obesity, and stress) that have been linked to the development of high blood pressure. Genetic studies, however, suggest that hypertension, or more correctly the predisposition for hypertension, is a heritable characteristic that results in high blood pressure when combined with environmental factors. Hypertension research therefore is both biomedical and behavioral.

The following are highlights of current advances in hypertension-related research supported by the National Heart, Lung, and Blood Institute (NHLBI). The National Center for Nursing Research and the Office of the Director, NIH, as well as the Institutes whose reports follow, also support research related to hypertension.

Newly Discovered Syndrome Involves Hypertension and Blood Cholesterol Disorders

Hypertension and blood cholesterol disorders (dyslipidemia) aggregate in families. Pathologic processes that lead to these two disorders may therefore involve shared genes, shared environmental factors, or a combination of both. Research on families living in Utah by NHLBI grantee Dr. Roger Williams at the University of Utah, Salt Lake City, has led to the description of a syndrome involving hypertension and dyslipidemia. The newly described syndrome, familial dyslipidemic hypertension (FDH), affected approximately 12 percent of patients with essential hypertension (that is, hypertension with no known cause) in the study population. Although FDH has been demonstrated in a limited number of families so far, if the findings from Utah turn out to be applicable to the rest of the Unites States, than FDH could affect 1 to 2 percent of the general population. Pedigree studies such as these are an important step in any attempt to understand the genetics of hypertension and atherosclerosis. Discrete, reproducibly measurable traits that can distinguish affected individuals from those not affected are central to the genetic linkage analysis that may follow.

Both Genetics and Environment May Influence Racial Differences in Hypertension

In a study of nearly 500 third-grade schoolchildren, Dr. Bruce Alpert, an NHLBI grantee at the University of Tennessee, Memphis, recently demonstrated that blacks had significantly greater heart rate and blood pressure reactivity than whites when challenged by a television video game. In a similar study in young adults, Dr. Kathleen Light, an NHLBI grantee at the University of North Carolina, Chapel Hill, observed that substantially greater blood pressure responses and blood pressure reactivity occurred in blacks compared to whites, when they were subjected to stress. Because there was no significant change in heart rate, the investigators reasoned that the potentially early disease state of black subjects was probably related to increased resistance in peripheral blood vessels.

In another study, Dr. Joel Dimsdale, an NHLBI grantee at the University of California, San Diego, found that, in normotensive and hypertensive individuals on low- and high-salt diets, norepinephrine, which elevates blood pressure, had different effects on blacks than on whites. The rate of rise in blood pressure was associated with increasing age, with black race, and with increasing levels of sodium in the diet.

Collectively, these studies suggest that blacks have a greater tendency than whites toward a "volume expanded" type of hypertension. The findings indicate an intersection between genetics and the environment, the genetic component relating to the impaired ability of some blacks to excrete salt, and the environmental influence relating to excess salt intake and increased stress among blacks. Such findings allow a more scientific approach to understanding the differences between hypertension in blacks and whites.

Consequences of Hypertension Are Less Severe in Premenopausal Women Than in Men

For some time it has been apparent that women, at least premenopausal women, have a lower cardiovascular disease frequency than men. The mechanisms of this protection, however, are not fully understood. Dr. Franz Messerli, an NHLBI grantee at the Ochsner Clinic in New Orleans, Louisiana, recently reported the results of investigations of 100 hypertensive women who were matched to 100 hypertensive men by mean arterial blood pressure, age, race, and body surface area. Women had a higher resting heart rate, higher pulse pressure, and lower resistance in the peripheral blood vessels than men with the same blood pressure. For any level of arterial blood pressure, total peripheral resistance (and therefore the risk of hypertensive cardiovascular disease) was lower in women than in men. The investigators concluded that women are "hemodynamically younger" than men of the same chronologic age.

This study provides a basis for the finding that essential hypertension is less lethal in women than in men. It would seem that, at least before menopause, gender influences not only blood pressure itself but also the consequences of high blood pressure.

Abnormality in Blood Vessel Relaxation Involved in Hypertension

The endothelial cells lining the inner surface of blood vessels secrete substances that regulate the activity of the smooth muscle surrounding the blood vessels. In experimental animals, this endothelium-mediated dilation of blood vessels can be impaired by acute and chronic hypertension.

Dr. Stephen Epstein, an NHLBI intramural researcher, has investigated the possibility that impaired endothelium-dependent blood vessel regulation may be a contributing cause of hypertension in people. To determine whether hypertensive patients have an endothelium-dependent abnormality in vascular relaxation, the forearm vascular responses of hypertensive and normal individuals to acetylcholine (an endothelium-dependent vasodilator) and to nitroprusside (an endothelium-independent vasodilator) were compared. The hypertensive patients had a normal response to nitroprusside but a significantly diminished response to acetylcholine. One way in which acetylcholine might act as a vasodilator independent of any effect on the vascular endothelium would be to inhibit secretion of norepinephrine, a vasodilator. However, the vasodilator effect of acetylcholine in patients was not blocked by the local infusion of alpha blockers, which block the vasodilator effect of norepinephrine. Thus, the experiments indicate that endothelium-mediated vascular relaxation is impaired in patients with hypertension and that this impaired process may contribute to or exacerbate the hypertensive process.

Newly Discovered Protein May Be Involved in Hypertension Development

In related studies, endothelin, a newly discovered protein secreted by the endothelial cells that line the blood vessels, has been shown to cause constriction of the vessels and is thought to play a significant

role in the control of blood pressure. Dr. John Burnett, Jr., an NHLBI grantee at the Mayo Clinic, Rochester, Minnesota, has studied the effects of endothelin in an animal model. He has shown that endothelin produces increased arterial blood pressure by causing increases in the resistance of peripheral blood vessels, and that their increased resistance is associated with increased resistance in blood vessels of the heart and decreased cardiac output. Blood flow and the rate of filtration in the kidney were markedly reduced, resulting in increased retention of salt.

Dr. Burnett's results show endothelin to be a potent vasoconstrictor that elevates blood pressure in association with marked decreases in heart and kidney function. It may function as a hormone that counters the effects of blood vessel relaxing factors also derived from endothelial cells, and it probably plays an important role in the control of blood pressure. Studies such as these point to the importance of the blood vessel endothelium as a source of regulatory substances that may be involved in the development of hypertension.

Opioid Neuropeptides Affect Blood Pressure Response to Stress

The most characteristic responses to stress involve the neurally mediated release of catecholamines (compounds that mimic the effects of impulses conveyed by the sympathetic nervous system) followed by the secretion of glucocorticoids (steroids affecting carbohydrate, fat, and protein metabolism) from the adrenal glands. This process is controlled by the hypothalamus and the pituitary gland, partly through the release of adrenocorticotrophic hormone (ACTH). It is becoming apparent that regulation of response to stress is additionally mediated by opioid neuropeptides, a class of substances released by the anterior pituitary gland.

Recently, Dr. James A. McCubbin, an NHLBI grantee at the University of Kentucky College of Medicine, Lexington, reported evidence that individual differences in blood pressure response to stress depend, in part, on the integrity of the opiate systems. Persons with high blood pressure may have a defect in opiate biosynthesis, a deficiency in the number or sensitivity of opiate receptors, or an overproduction of a natural opiate antagonist. Particularly interesting is the finding that blood pressure as well as the secretion of ACTH in response to stress is altered in hypertensive young adults. Dr. McCubbin's data and related findings by other investigators suggest that reduced influence of opioid pathways during stress may underlie the exaggerated reactivity observed in young adults at increased risk for development of hypertension and may therefore suggest an additional target for development of interventions.

Studies of Salt Sensitivity Include Investigation of Sodium Excretion by Kidney and Effect of High-Salt Diet on Catecholamine Metabolism

Salt and water excretion by the kidney has a contributing role in the development and control of hypertension. Dr. Mark Knepper, an NHLBI intramural researcher, is studying the mechanism of salt excretion by the kidney. A new technique for measuring sodium and potassium in very small amounts of fluid, which allows measurements in samples taken from

different parts of the kidney, shows that there are two different and parallel pathways for the transport of sodium.

Dr. David Goldstein, another NHLBI intramural researcher, studied the effects of high salt diets on metabolism of two catecholamines, dopa and dopamine, in rats given large amounts of salt. Urinary excretion of both dopa and dopamine was found to increase markedly in salt-loaded rats. This is consistent with the concept that metabolism of these catecholamines in the kidney plays an important role in the regulation of sodium levels. Direct measurements of blood levels of the catecholamines showed that their increased secretion in the urine was not due to an increase in their concentration in the blood, indicating that the kidney synthesizes dopa and dopamine in rats given large amounts of salt.

Methionine-Supplemented Diet Protects Kidneys of Hypertensive Rats

Dr. Victor Ferrans, an NHLBI intramural researcher, studied the morphology of the kidney and heart of 10-month-old stroke-prone, spontaneously hypertensive rats that had been fed one of three diets for 9 months: standard diet, low-protein diet, or high-methionine diet. The low-protein diet caused earlier development of more severe hypertension and led to earlier and more frequent development of stroke. These patterns were reversed by addition of the amino acid methionine to the diet. For all three groups, the degree of cardiac enlargement and fibrosis, thickening of intramyocardial arterioles, and the presence of inflammatory cells were the same. However, whereas the kidneys of the rats fed the low-protein diet showed marked abnormalities, the kidneys of the rats fed a diet supplemented with methionine were essentially normal. Thus, supplement of the normal diet with methionine seemed to protect the spontaneously hypertensive rats against kidney damage that occurs with a normal diet alone. It is not yet known if this is due to a direct effect of the methionine on hypertension or to a protective effect against the kidney damage caused by prolonged hypertension.

National Institute of Neurological Disorders and Stroke

The National Institute of Neurological Disorders and Stroke (NINDS) supports research on hypertension, a condition associated with 70 percent of the hemorrhagic strokes that occur in the United States.

Anatomical Differences May Reflect Nerve Tract Reactions

Two important brain nerve tracts, the centrum semiovale and the corpus callosum, react differently to hypertensive conditions: vascular changes are commonly seen in the former, but not in the latter. Dr. Dixon Moody, an NINDS grantee at the Bowman Gray School of Medicine in Winston-Salem, North Carolina, has uncovered accompanying anatomical differences: the centrum semiovale is supplied by long, convoluted arteries; the corpus callosum, by short arteries. It is possible that the extra length -- as well as surface area -- of the centrum semiovale arteries makes this tract more susceptible to hypertension-related changes. Dr. Moody, a neuroradiologist, is also pioneering the use of new technologies that will help to identify diseased brain arteries.

Stroke Severity, but Not Occurrence, May Be Affected by Hypertension

A decrease in the number of deaths from stroke over the last 16 years has generally been attributed to better control of hypertension. Dr. Philip Wolf, an NINDS grantee at the Boston University School of Medicine, has examined trends in the incidence of stroke as well as stroke mortality using three decades of data from the Framingham Heart Study. He found that strokes occurred three times more frequently among hypertensive men than among men with normal blood pressure. He also discovered that although the number of fatal strokes has declined substantially -- particularly in men -- the overall incidence of stroke has not. Dr. Wolf has suggested that hypertension treatment in the general population appears to affect the severity of stroke rather than its rate of occurrence.

National Institute of Child Health and Human Development

The National Institute of Child Health and Human Development (NICHD) supports a number of research projects on hypertension as it relates to maternal health care and pregnancy outcome. One possible complication in pregnancy, pre-eclampsia, is the development of increased blood pressure. If left untreated the condition can develop into full-blown eclampsia which, in a small number of cases, can lead to convulsions and coma. In the most severe cases, eclampsia can pose a serious threat to the lives of both the mother and the fetus.

Pre-eclampsia complicates about 5 percent of pregnancies, usually occurring sometime during the last 3 months of pregnancy. Although the cause of the syndrome is unknown, doctors previously believed that some unidentified toxic substance was responsible. This theory has since been ruled out, but physicians agree that pregnant women should receive regular medical care to check for early warning signs of this "silent" condition.

Researchers Study Development of Uterine and Placental Arteries

Many gaps exist in our understanding of the development of the uterine and placental arteries in primates, especially in the cellular mechanisms by which invasion, destruction, and replacement of the cells constituting these structures are carried out. It has been observed that pregnancies complicated by pre-eclampsia alone, or pre-eclampsia with essential hypertension, exhibit less structural modification of the arterial walls, thereby compromising the greater volume of blood flow required during pregnancy by the developing fetus. Using the rhesus monkey, a species with many placental anatomical similarities to humans, Dr. Barry F. King and his colleagues at the University of California are studying the development of the uteroplacental arteries in primates.

Placental Immunology May Become Disordered in Hypertensive Conditions Such As Pre-eclampsia

Placental immunology is being examined by Dr. Elliott Main of the University of California at San Francisco in an attempt to understand why placental development is abnormal in patients who develop pre-eclampsia. Normally, trophoblast (placental) cells have no cell-surface antigens to which the mother's immune system can react. Trophoblast cells from pre-eclamptic pregnancies, however, have such antigens, thus setting the stage for impaired placental development. This research is designed to help researchers understand how this antigen expression is regulated at the cellular level and how this regulation may become disordered in hypertensive conditions such as pre-eclampsia.

Clinical Trial Focuses on Role of Aspirin in Treatment of Pregnancy-Associated Hypertensive Disorders

Pregnancy-associated hypertensive disorders (PAH) are responsible for numerous maternal deaths and a substantial proportion of perinatal deaths in the United States. Investigators will evaluate the role of aspirin in preventing PAH and try to determine if it is possible to predict which

women will develop PAH. Dr. John C. Hauth and his colleagues at the University of Alabama at Birmingham are conducting a randomized double-blinded trial on 600 otherwise healthy nulliparous women. Beginning at 24 weeks' gestation, the subjects will receive either low-dose aspirin or a placebo. Maternal blood samples will also be used as a resource for future analyses of other potential predictive markers of PAH.

National Institute on Aging

The National Institute on Aging (NIA) supports a number of studies that examine hypertension, a condition existing in half of all people over 65.

Study Focuses on Isolated Systolic Hypertension in Older Persons

Dr. William Applegate, an NHLBI grantee at the University of Tennessee Center for Health Sciences in Memphis and a member of the NIA Advisory Council, recently analyzed the benefits and risks of the most common therapies for older people suffering from hypertension. Dr. Applegate suggests that physicians take special care with older patients and watch for the side effects of the medications used to control blood pressure. At least 40 percent of hypertensive older people are now being treated with drugs which have the potential for affecting their quality of life, mood, and energy level.

One of the studies that Dr. Applegate discusses is the Systolic Hypertension in the Elderly Program, jointly supported by the NIA and the NHLBI, which examines isolated systolic hypertension (ISH). ISH is defined as a systolic blood pressure reading of more than 160 mm Hg with a diastolic blood pressure reading of less than 90 mm Hg. The results of SHEP's double-blind intervention trial are expected in the next 2 years, and will provide definitive recommendations on ISH treatment, including benefits and side effects, in older people.

In people over age 65, ISH more than doubles the risk of stroke. In screening for the SHEP pilot study, the prevalence of ISH was about 10 percent of persons over 70 years old; 20 percent of persons over 80 years old have this form of high blood pressure.

Among drug therapies, diuretics are the most effective type of drug used in lowering blood pressure in older people. However, Dr. Applegate indicates that a variety of other classes of antihypertensive medications are effective in older patients.

The most commonly reported side effects from hypertensive medications are: problems with balance and dizziness upon standing up; confusion and depression; delayed mental reaction time; potential alterations in blood flow to the brain or kidneys; urinary incontinence; and sexual dysfunction.

Older persons do not always experience side effects from the medications. A pilot study of SHEP suggested that ISH can be fairly easily treated with drugs in older people, with relatively low rates of adverse responses. In a separate study of older patients who were otherwise healthy, drug treatment revealed that harmful side effects were no more common in older than younger patients. But little data have been collected on the impact of such medications in frail older people who suffer from other serious illnesses.

In the pilot study for SHEP, 551 subjects with ISH were treated with a diuretic and an additional drug if needed, and compared with a placebo

group. Seventy-five percent had their ISH controlled with the diuretic alone. There were no substantial differences between the control and treatment groups in terms of toxic reactions to the drugs.

Dr. Applegate also mentions types of therapy that do not involve drugs for older hypertensive people. These interventions include weight loss for overweight people, sodium restriction, reduction or cessation of alcohol consumption, regular aerobic exercise, and relaxation therapy.

Treatment of hypertension in older people may become a matter of individual choice in weighing the advantages of a slightly extended lifespan against the disadvantages of side effects that can include diminished emotional or cognitive functions, mobility and balance, or sexual interest.

Division of Research Resources

Shared research facilities provided by the Division of Research Resources (DRR) support a variety of research projects focused on hypertension. Several of these studies, aimed at understanding the basic mechanisms of high blood pressure, are building the foundation for more effective treatments.

Sophisticated projects such as these require a research infrastructure that supports collaboration among the medical disciplines. General Clinical Research Centers (GCRCs) provide this infrastructure for research on both children and adults. Specifically, they provide patient research facilities, computerized data management and analysis, as well as research nurses, dietitians, biostatisticians, and specialized laboratories for the translation of basic and clinical research into medical practice.

Sodium Sensitivity of Blacks and Whites Compared

Recently, GCRC grantees found information that may help explain why hypertension is more severe and more prevalent in blacks than whites. It may also explain why blacks do not respond to certain therapies that are effective in whites.

Grantees Dr. Michael Ziegler at the University of California in San Diego and Dr. Robert E. Graham at the Massachusetts General Hospital in Boston examined how dietary salt intake affects the sensitivity of hypertensive men to hormones released from nerve endings. Those hormones are involved in the control of blood pressure.

The investigators found that high-salt diets increase the sensitivity of black hypertensive men to these hormones, but have the opposite effect on white hypertensive men. The GCRC grantees in San Diego and Boston demonstrated a significant three-way interaction among the factors of race, dietary salt, and hypertension. They noted that the difference in sensitivity may explain why blacks do not respond to certain blood pressure therapies that are effective in whites.

The mechanisms of hypertension in blacks and whites were further explored at the University of Tennessee GCRC in Memphis by DRR grantee Dr. Jay Sullivan and his colleagues. They studied the responses to sodium depletion and repletion in 92 healthy and 65 borderline hypertensive subjects.

The prevalence of sodium sensitivity was higher in blacks than in whites and greater in hypertensives than in healthy subjects. The grantees found that sodium sensitivity was associated with decreased plasma renin, an enzyme released by the kidney, and reduced blood levels of aldosterone, a steroid hormone secreted by the adrenal gland.

According to Dr. Sullivan, the data suggest a genetic basis for the response to sodium. If so, the knowledge could lead to the development of genetic tests to identify people who are sensitive to sodium and who should, therefore, avoid eating salt.

Converting Enzyme Inhibitors Correct Renal and Adrenal Defects in Some Hypertensives

DRR grantees Drs. Gordon H. Williams and Thomas J. Moore at the Brigham and Women's Hospital GCRC in Boston found that a relatively new class of antihypertensive drugs correct defects in the kidney and adrenal glands. These drugs, called converting enzyme inhibitors (CEIs), lower blood pressure in about 50 percent of the patients with hypertension of unknown cause associated with normal or high levels of renin.

CEIs are known to block the generation of angiotensin II, a potent blood vessel constrictor that can increase blood pressure. Studies conducted by Drs. Williams and Moore demonstrate that CEIs correct the renal abnormality and adrenal defect in some hypertensives without affecting levels of circulating angiotensin II. This observation supports the belief that there is an abnormal response of the tissue in these subjects to the renin-angiotensin system, according to Dr. Williams.

Outlook

Rapid developments in molecular and cellular biology, especially in the genetics of hypertension, can be expected to continue in the next decade. The relative ease of production of such powerful tools as specifically designed retroviral systems and transgenic animal models, coupled with other types of analysis based on family pedigrees and DNA analyses, at last provide the wherewithal to begin to understand the genetic basis of this complex disorder. The immediate consequences of such an understanding will be the ability to detect, by genetic markers, those individuals most likely to become hypertensive, at a time before there is any detectable rise in blood pressure, and at a time when preventive measures can be most effectively taken.

One major area requiring increased attention is the developmental biology of the vasculature. Exploration at the molecular level of the relationships among cell growth, division, migration, and differentiation in developing blood vessels is likely to provide the basis for understanding fundamental mechanisms that underlie cardiovascular diseases, including hypertension. For example, little is known about how and when the walls of the blood vessels are formed, or how these are remodelled to produce the thickened structures of the hypertensive vessels. Recent advances in molecular embryology have begun to allow the identification and tracing of cell lineages and of the specific genes involved in the control of development. These approaches must now be applied to a study of the development of the vasculature, and to investigation of difficult questions about hypertension that remain unanswered so far.

Although it is important to pursue the many areas of basic science relating to hypertension, applied and clinical studies are also important, particularly for advancing knowledge on treatment and control of hypertension. Hypertension is principally a human disorder and clues to its causes continue to be disclosed by epidemiologic studies of populations, which generally assess nongenetic precursors. From these studies, a number of valuable nutritional recommendations are emerging of relevance to the control of elevated blood pressure. Clinical trials have had a profound effect on improvement in identification and clinical management of hypertension. This success has provided the incentive to address new issues, such as primary prevention, the discordance between predicted and observed coronary artery disease when blood pressure is lowered, and the efficacy of alternative interventions for subjects at high risk. Community programs, with added emphasis on minority groups, the young, and the elderly, all of whom pose special problems in relation to hypertension management, are also components of the spectrum of approaches to the eventual control of human hypertension.

CENTERS FOR DISEASE CONTROL

National Center for Health Statistics

HYPERTENSION

The total prevalence of hypertension in the United States population 18-74 years of age was determined in the National Health and Nutrition Examination Survey (NHANES I) of 1971-74 with further data on hypertensive heart disease obtained on adults 25-74 years of age. These NHANES studies also permit comparison of blood pressure levels over time, providing population-based broad program evaluation information as well as data for epidemiologists studying the decrease in cardiovascular-related mortality rates.

In the second National Health and Nutrition Examination Survey (NHANES II), data on the prevalence, severity and person's awareness of their hypertensive condition was again collected as an aid to the National Hypertension Control and Research programs in monitoring progress in the control of this condition.

Published data from the NHANES II, which covered the period 1976-80, indicate that there was increased awareness, treatment, and control of hypertension during the 1970's. Approximately 25.1 million United States adults ages 25-74 years were estimated by examination and interview to either have elevated blood pressure or be on hypertensive medication, a prevalence of 22.0% in that age group. The prevalence of hypertension among adults has not changed significantly since 1960-62 except for an increase among white men. However, among those with hypertension, the percent never diagnosed by a physician as having hypertension or high blood pressure has dropped significantly. This increase in awareness has been accomplished by an increase in the proportion of hypertensives who reported they were currently taking antihypertensive medication.

Data on hypertension were also collected in Hispanic HANES (1982-84). The prevalence of hypertension among Mexican American, Cuban, and Puerto Rican men was estimated to be 16.8%, 22.8%, and 15.6% respectively. Rates for women were 14.1%, 15.5%, and 11.5% for Mexican Americans, Cubans, and Puerto Ricans respectively.

Awareness of their condition among hypertensive women in the three Hispanic subgroups was over 95%. Hypertensive men in the three groups were less often aware of their condition, with levels of awareness being 67.9%, 87.2%, and 78.7% for Mexican-American, Cuban, and Puerto Rican men respectively.

Levels of control of hypertension among women, Mexican Americans, Cubans, and Puerto Ricans were found to be 43.6%, 29.5%, and 41.9% respectively. Hypertensive men in the three Hispanic subgroups were found to have lower level of control with 22.6%, 26.1%, and 29.1%

for Mexican-American, Cuban, and Puerto Rican men respectively.

Data on hypertension are being collected in NHANES III, which began in October 1988.

The National Ambulatory Care Medical Survey (NAMCS), another program of the Center, reported that patients with essential hypertension made an estimated 26 million visits to office-based physicians in 1985. During these visits there were about 39 million mentions of drugs, either new or continued, offered by the physician, for an average of 1.5 drug mentions per visit. The NAMCS was done annually from 1973 through 1981. The most recent survey was conducted in 1985, and the next survey is planned for 1989.

In 1988, the National Health Interview Survey (NHIS) collected data on the prevalence of high blood pressure (hypertension) for the civilian, noninstitutionalized population of the United States. The total number of persons of all ages who reported having high blood pressure was 29,257,000. Of the different age groups, the highest rate was for those 65 years of age or older (373.0 per 1,000 persons). The rate for female age groups combined reporting high blood pressure was higher than for males; 131.5 for females and 110.7 for males per 1,000 persons, respectively. The NHIS has been collecting hypertension data on a continuing basis since 1978. In addition, during 1974, the survey collected extensive supplemental data on hypertension for persons 17 years of age and over. The National High Blood Pressure Education Program was a major impetus for collection of these data to aid in their goal to lower the morbidity and mortality associated with hypertension. A detailed discussion of the extent of the problem of hypertension, including factors which increase the risk of hypertension, appeared in Health, United States, 1976-1977.

According to the 1987 National Hospital Discharge Survey, an estimated 302,000 patients were discharged from short-stay hospitals in the United States with a first-listed diagnosis of hypertensive disease. The average length of stay for these patients was 5.7 days. Females accounted for 59 percent of the discharges and patients 45 years and over accounted for 80 percent of the discharges.There were an additional 3.3 million hypertensive disease diagnoses (other than first-listed). Although some of these diagnoses were associated with patients who had a first-listed diagnosis of hypertensive disease, the majority of these patients had a non-hypertensive disease as first-listed diagnosis.

INFANT MORTALITY
Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
Public Health Service:					
Health Resources and Services Administration 1/	$38,680,000	$278,433,000	$291,006,000	$309,698,000	$360,765,000
Indian Health Service.....	183,625,000	160,518,000	169,479,000	180,890,000	191,656,000
Alcohol, Drug Abuse and Mental Health Administration 2/.....	38,042,000	97,133,000	175,702,000	289,858,000	315,197,000
Centers for Disease Control.....	8,095,000	22,572,000	30,186,000	42,907,000	70,804,000
Agency for Health Care Policy and Research.....	—	319,000	925,000	900,000	900,000
National Institutes for Health.....	88,902,000	101,688,000	119,585,000	132,131,000	141,757,000
Total PHS	$357,344,000	$660,663,000	$786,883,000	$956,384,000	$1,081,081,000

1/ Assumes that approximately 50 percent of community Migrant Health Centers and Health services in pubic housing programs support activities for mothers and children

2/ Amounts for FY 1989, 1990, and 1991 include estimates for the block grant.

HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Health Care Delivery and Assistance

INFANT MORTALITY

The purpose of the infant mortality initiative is to make comprehensive perinatal care services available to pregnant women in underserved areas with high infant mortality rates.

To improve the pregnancy outcomes and health status of underserved women and infants, in Fiscal Year (FY) 1989 $20 million in grants was awarded to fund comprehensive perinatal delivery systems stressing coordinated-case management in community/migrant health centers(C/MHC). Two hundred six C/MHCs were funded under the Comprehensive Perinatal Care Program to provide case managed, care coordinated services to an estimated 52,000 mother infant pairs.

The services of the program encompass: (1) systems of care designed to incorporate case management into the delivery model and enhance health services that are responsive to the medical, social, and behavioral needs of pregnant women and infants; (2) maintenance of current perinatal capacity within C/MHC through efforts to retain or recruit obstetrical health care providers to include, among other, obstetrician/gynecological and family practice physicians and certified nurse midwives; and (3) expansion of capacity to evaluate progress of current and expanded perinatal interventions based on health outcomes and health status (i.e. measures such as low birth weight teenage pregnancy rates, and infant mortality).

In order to enhance case management activities, and in turn maximize positive birth outcome, support has been provided to expand C/MHC services through the addition of staff for patient education and outreach. Case management activities include, but are not limited to : casefinding; reducing nonfinancial barriers to care, such as translation assistance; reducing financial barriers though assistance in enrollment in Medicaid; and providing patient education regarding related medical and health services, assistance and resources that are available in community (AFDC, WIC, EPSDT, and housing), and how to gain access to them.

In FY 1990 activities will focus on enhancing the capacity of C/MHC perinatal programs to offer the necessary comprehensive, case-managed services necessary to impact on adverse birth outcomes. The capacity of these programs to serve additional women in need will also be enhanced.

The 1991 request includes $2,000,000 for a one time grant to support the purchase of up to 75 vans to be used in the transport of pregnant women and mothers to community health centers for perinatal services as part of the Secretary's initiative to reduce infant mortality. By assisting in the provision of transportation of pregnant women and mothers to and from the centers it is hoped that one of the barriers to improved perinatal care, transportation difficulties, can be reduced.

HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Maternal and Child Health and Resources Development

INFANT MORTALITY

Infant Mortality and low birth weight are addressed in several ways with SPRANS funds. A number of Maternal and Child Health Improvement Projects address various methodologies to improve the utilization and content of prenatal care, risk appropriate care, reduction of behavioral risks, care coordination and local Infant Mortality reviews. Research projects support examination of issues and factors directly concerned with or related to Infant Mortality. Funds have also supported a number of local/state efforts at problem identification, analysis and evaluation. Efforts have also been directed to improve public/private coordination and collaboration as well as public/professional communication and education.

The Maternal and Child Health block grant program contributes to infant mortality in addition to improving health for mothers and children. The exact amount for infant mortality cannot be ascertained based on available data. The amount shown includes that portion of special projects (SPRANS) that directly relates to infant mortality.

In Fiscal Year 1991 a special grant initiative, "one-stop shopping", will provide aid to States and community based organizations to further enhance access to prenatal and post natal care and related services. An estimated 75-100 projects are expected to aid in restructuring and reorganizing the application and health services delivery process as it relates to the delivery of quality health care to and for pregnant women and infants. Preference for these projects would be given to States and communities with above average infant mortality rates and substantial minority health disparities.

HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Health Professions

Infant Mortality

In FY 1989, the Advanced Nursing Education Program awarded 13 grants totaling $1,714,699 designed to prepare master's and doctoral level nurses to address the problems of mothers and children in acute care and other settings. Preparation of teachers and researchers in this important area also occurs in these educational programs.

The Nurse Practitioner and Nurse Midwifery Program awarded $5,281,278 to 30 projects to support preparation of nurses who are able to serve as nurse midwives, obstetrical and gynecological practitioners, and pediatric practitioners. In all cases, these nurses focus on patient teaching, guidance, counseling and health screening activities.

Public health funds have been used to support traineeships to improve administration and competency of personnel in maternal and child health programs. In FY 1988, $127,190 was awarded for traineeship support in maternal and child health.

An estimated 587,690 individuals benefitted from the Area Health Education Center programs targeted for training in maternal and child health. A total of $416,900 was awarded among 12 grantees reporting activities in this area. The largest award of $125,000 was to the University of Arizona for its statewide project.

Area Health Education Center projects at Michigan State University and the College of Osteopathic Medicine of the Pacific both have developed training and patient education programs in this area. A total of 220 individuals will be affected by these program initiatives and $3,000 was specifically requested for Sudden Infant Death Syndrome activities.

Four Family Medicine Predoctoral program grantees and nine Graduate Training program grantees indicated training in maternal and child health. An estimated 107 residents will benefit from this training.

One grantee under the section 788(c) Preventive Medicine Residency Training program will offer seven trainees a curricular component which emphasizes maternal and child health issues.

A total of $199,420 was awarded to six of 35 Physician Assistant Training programs which indicated maternal and child health care activities. It is estimated that 1,612 trainees will have educational experience in this area. The University of Colorado Child Health Associate Program for training physician assistants received $165,000 for development of an entire curriculum in child health (prenatal through adolescence). The University of Colorado provides exposure to Sudden Infant Death Syndrome for 25 of its trainees.

Maternal and child health issues related to HIV/AIDS are included in the training offered by six AIDS Regional Education and Training Centers program grantees.

INDIAN HEALTH SERVICE

Infant Mortality

The reduction of infant mortality among American Indians and Alaska Natives (AI/AN) is an important objective of the Indian Health Service (IHS). Through direct and contract programs, prenatal, perinatal, neonatal and post-neonatal care, are provided to mothers and infants. Community based indigenous health workers, primary care professionals, and secondary and tertiary based specialists work together in a regionalized system to provide this comprehensive care.

Maternal and Child Health is not an IHS line item. However, based on the numbers of deliveries, newborns, infant care, prenatal care and certain specific prevention programs (Alaska Prenatal initiative, Haemophilus influenzae prevention and FAS prevention) cost estimated can be derived. The IHS expended $169,479,000 in Infant Mortality prevention in FY 1989. Since IHS program activities are primarily rural, the difficulty and cost of delivering a reasonably high technical level of health care increases.

The latest (FY 1985) AI/AN infant mortality generally was 9.7 deaths per 1000 live births. This is a 48 percent decrease since 1974 and is 0.9 times the rate for U.S. All Races. Data from IHS Service Areas show an average infant mortality rate of 11.8. A more detailed analysis of this data show two important facts: (1) AI/AN infants are at a higher risk from 28 days to 11 months of age, and (2), seven of the 12 IHS Areas have infant mortality rates above the rate for U.S. All Races.

Efforts to reduce infant mortality must target high risk population subsets. Therefore, program activities to reduce infant mortality in the future will be strengthened to focus on the following:

1. Adolescent pregnancy rate (currently 20 percent of AI/AN births are to mothers less than 20 years of age)

2. Fetal alcohol syndrome rate (date gathered from some areas show rates from 6 to 10 per 1000 live births)

3. Sudden Infant Death Syndrome (SIDS) (in regions of high infant mortality the post-neonatal deaths due to SIDS is very high)

4. Prenatal care (significant high risk population subsets do not participate in prenatal care)

ALCOHOL, DRUG ABUSE AND MENTAL HEALTH ADMINISTRATION

National Institute on Drug Abuse

INFANT MORTALITY

Approximately six million women of childbearing age in the United States have tried an illicit drug at least once in their lifetime. Historically, obstetrical and neonatal complications have been reported with the use, during pregnancy, of alcohol, opiates, and other drugs; an added concern today is perinatal transmission of HIV as a consequence of IV drug abuse by pregnant women or their sexual partner. Although precise data on the prevalence and incidence of drug use during pregnancy do not exist, it is estimated that as many as 375,000 infants may be affected by in-utero exposure to drugs each year in the U.S. A pilot study of 36 mainly urban hospitals in the U.S., which account for some 155,000 births annually, found that on average, 11 percent of pregnant women abused drugs, most frequently cocaine.

Over the past several years, the National Institute on Drug Abuse (NIDA) has expanded its research program on the effects of maternal drug use to:

1) identify the risks to the mother and child of maternal drug use both before and during pregnancy;

2) improve treatment programs for pregnant women;

3) develop new drug abuse treatment medications that will diminish risk to the fetus;

4) develop treatments for drug-exposed infants; and,

5) develop prevention programs targeted to women of childbearing age.

Cocaine: Obstetrical and neonatal effects such as spontaneous abortions, premature delivery, low birth weight infants, small for gestational age, and neurodevelopmental defects such as impaired memory, intelligence, and motor coordination problems, have all been associated with in-utero cocaine exposure. Sudden infant death syndrome (SID) also is associated with maternal cocaine use. This listing of effects is derived from case reports and small pilot studies; larger studies are needed to confirm them.

Recent studies have shown that cessation of cocaine use early in pregnancy (i.e., the first trimester) may improve obstetric outcomes but does not diminish risk of neurological impairment. Cocaine-exposed infants are slow to respond, demonstrate impaired motor coordination, and are less alert than non-cocaine exposed infants. There are rare cases of seizures with abnormal EEGs,

and cerebral infarction (stroke) in infants born to mothers who used cocaine throughout pregnancy. NIDA-funded investigators at Northwestern University Medical School have examined the effects of cocaine use on pregnancy outcome and the neonate. In the past year, published articles have documented: 1) an increased rate of genitourinary tract malformations in cocaine-exposed infants, 2) toxicological effects of cocaine passed via maternal breast milk, and 3) the effects of temporal patterns of maternal cocaine use on pregnancy outcome and the neonate.

The delayed neurodevelopment of infants exposed to cocaine and marijuana in-utero also has been reported by NIDA grantees at the Boston University School of Medicine. In a study of 1,226 low socioeconomic class pregnant women, 27 percent used marijuana and 18 percent used cocaine during pregnancy. In comparison to infants not exposed to drugs, the use of marijuana was associated with lower infant birth weight, and decreased length; cocaine use had more pronounced effects, including low birth weights, shorter infants, and smaller head circumferences. Neither drug was associated with shorter gestation or congenital anomalies. The investigators found that 16 percent of the women denied using marijuana and 24 percent denied using cocaine, even though their urine toxicology was positive. Such evidence that self-reports may not be totally reliable predictors of drug use during pregnancy suggests the usefulness of routine testing.

Marijuana: NIDA grantees have reported that marijuana use during pregnancy, regardless of time of use during pregnancy, decreases the gestational age, decreases the amount of sleep by the neonates, increases their activity, and increases the number of tremors and startles (a possible delayed neurodevelopmental effect). Preliminary analyses of a multi-year study have shown that long-term marijuana use by pregnant women impairs, in a dose-dependent fashion, their children's memory up to age four. This project is continuing to examine the long-term effects of marijuana, alcohol and tobacco use during pregnancy on auditory functioning, attention deficits, cognitive performance, verbal skills, sensory skills, kinesthetic functioning, memory, intelligence, and academic readiness in both neonates and growing children up to age six.

Alcohol: Alcohol use during pregnancy is associated with the fetal alcohol syndrome (FAS), as well as with premature delivery of low birth weight infants. Maternal use of alcohol and tobacco and/or marijuana during pregnancy is associated with a decreased amount of sleep and an increased number of arousals in the newborn, suggesting that the neurodevelopmental effects of these drugs may be similar.

PCP: A NIDA grantee studying children prenatally exposed to phencyclidine (PCP) found that they show striking deficits when compared matched control babies whose mothers' did not use PCP. The PCP exposed children had significantly lower developmental scores and almost all of them had some ataxia, intentional

tremors, and a static stare that resembles a type of autism. When the PCP-abusing mothers were subjectively evaluated, they appeared immature, less sensitive, and less accepting of their children than the control mothers.

The impact of these findings is potentially enormous. Children of substance-abusing parents live in unstable, often dangerous environments, cared for inconsistently by parents impaired by chronic drug abuse. Postnatal environmental factors and the possibility of prenatal biological impairments pose grave risks to the children's health and development.

HIV Transmission and AIDS: The CDC reports that approximately 30 percent of all AIDS cases are among intravenous drug abusers. Heterosexual intravenous drug abusers account for about three-quarters of these, with homosexual and bisexual intravenous drug abusers account for the remainder. Among male AIDS cases, 17 percent were heterosexuals who reported using needles, at least once prior to developing AIDS, for self-injection of drugs not prescribed by a physician. Fifty-two percent of all female AIDS cases reported such a drug abuse history.

Although only 5-percent of AIDS cases can be attributed solely to heterosexual contact, many of these can be directly linked to intravenous drug abusers. Likewise, 81 percent of pediatric AIDS cases can be attributed to a mother who uses drugs intravenously or whose sexual partner does. AIDS, it appears, is occurring among the heterosexual partners and children of intravenous drug abusers in epidemic fashion.

Perinatal AIDS--already the ninth leading cause of death among children one to four years of age--is rising rapidly as a cause of death among children. If current trends continue, AIDS could be among the top five causes of death for young children within the next three to four years.

Currently, NIDA is funding 41 demonstration research projects, at 63 sites, offering both comprehensive AIDS prevention programming and targeted AIDS prevention. While all of the projects deal with perinatal AIDS prevention by educating and treating women of childbearing age, two projects in northeastern cities are specifically targeted to pregnant women at risk for HIV infection; the projects involve outreach, preventive counseling, and education.

Basic Biological Studies: All major classes of drugs of abuse cross the placenta and influence the development of the fetus, the course of pregnancy, and subsequent human development. Little is known, however, of the magnitude, mechanisms, and duration of the direct effects of drugs on the fetus. Basic biological studies under development include genetics; neuroendocrine effects on the cardiovascular, immune, and other organ systems; pharmacokinetics; and neuroendocrinology, to determine the functional significance of reported alterations in

hormone profiles in neonates exposed prenatally or perinatally to drugs.

Urgent questions exist regarding the extent to which children of drug-abusing parents are more likely to engage in drug abuse by virtue of a mixture of genetic, neurobiological, familial and other environmental factors. Research to identify the behavioral and biological variables that control each individual step in the cycle of events leading to drug-induced toxicity in the newborn and, thus, to intergenerational transmission of risk is planned. Information gained will contribute to prevention/intervention efforts, both to reduce the incidence of newborns affected by drug toxicity and to minimize short- and long-term consequences on the child.

Although effects of in utero drug exposure--including withdrawal syndromes--have been identified, systematic information is lacking about the nature of these changes and how they may be affected during the course of childhood development. This information, needed to guide clinical management of the newborn and to develop assessment and intervention procedures to prevent or ameliorate developmental delays and disabilities, is being sought by NIDA investigators. Of particular interest are studies that will analyze the mechanisms and behavioral consequences of drug-induced CNS (central nervous system) toxicity, especially with respect to defining the period of vulnerability of the developing nervous system.

Information regarding fetal and offspring consequences of drug abuse by fathers' is virtually nonexistent. However, data from animal studies suggest that morphine administration in the male rat just prior to and during puberty significantly reduced male hormone levels in their male progeny. These effects persisted through adulthood, suggesting that exposure to opiates early in life may have long term effects on the development of male offspring.

Prevention and Intervention: The overall goal of NIDA's research program is to prevent drug abuse at or before conception; and, if that fails, to intervene to prevent developmental difficulties and complicating familial and environmental risk for the child.

Drug abuse by one or both partners may influence: (a) the likelihood of sexual activity that results in pregnancy; (b) the choice of the sex partner; (c) the fact that the sexual activity occurs in the absence of adequate protective measures against not only pregnancy but also sexually transmitted diseases; (d) the time period until the pregnancy is confirmed and, thus, adequacy (or omission) of prenatal care; and, (f) the behavior of one or both parents which places the pregnancy or infant at risk. Studies leading to the development of strategies to prevent high risk sexual behaviors, particularly among adolescents, are being sought.

Few drug abusing women seek or receive prenatal care and, with the exception of drug abuse treatment services, few health care professionals, clinics, or hospitals have the training and resources to identify and treat these women. Drug treatment programs, moreover, are ill-equipped to treat pregnant women. Treatment tends to focus on the mother's addiction rather than on the pregnancy and the child; treatment of the infant tends to focus on withdrawal rather than the assessment of more subtle behavioral and functional disorders.

NIDA is beginning to address these gaps in maternal and infant care through prevention research programs. NIDA seeks to develop new and improved forms of preventive, therapeutic and support programs that address not only the physiological effects of addiction, but other medical and psychosocial consequences as well. Clearly the goals here are to reduce the incidence of maternal drug use during pregnancy, and improve the health and general well being of both mother and child during and after the pregnancy.

Researchers are seeking ways to remove the barriers to treatment that certain women currently faced, particularly those who are be very young, unmarried, socially isolated, and/or struggling with drug-related problems. Programs that plan for or provide extensive prenatal medical care, including a safe detoxification regimen, crisis counseling, support group activities, and "headstart" parent training are of particular concern. In addition, because drug withdrawal during pregnancy can be life-threatening for the fetus, NIDA is planning research on clinical management approaches to reduce maternal drug intake and to retain the drug-addicted mother in a treatment program

Finally, studies that identify the full range of the consequences of drug abuse for the unborn and newborn child are essential. Once we gain such an understanding, we may develop strategies to cope with the complications of delivery by an addicted mother and improve the newborn's chance of normal cognitive and physical development. In addition, NIDA seeks to explore special child-rearing practices and develop ways to address the many exceptional needs of children born to addicts, who are developmentally compromised, indeed, perhaps even handicapped, from the outset because of their mothers' addictions.

Office for Substance Abuse Prevention

INFANT MORTALITY

While statistics on the number of women who abuse drugs during pregnancy are hard to obtain, a 1988 survey by the National Association for Perinatal Addiction Research and Education found that, of 37 hospitals polled throughout the country and representing approximately 155,000 pregnancies annually, on average, 11 percent of the pregnant women used heroin, methadone, amphetamines, PCP, marijuana, and most commonly, cocaine. Extrapolating from this sample, the researchers estimate that each year as many as 375,000 infants may be affected by their mother's drug use.

The use of any drug during pregnancy introduces an element of risk for both pregnant mother and the fetus. In a recent study at the Northwestern University's Perinatal Center for Chemical Dependence, clinical investigators found that women injecting cocaine intravenously during pregnancy immediately experienced complications, including premature separation of the placenta from the womb, which causes hemorrhaging that threatens the lives of both mother and fetus. In a separate study, cocaine-addicted women were found to be twice as likely to suffer premature separation of the placenta as were women dependent on other drugs and four times as likely as drug-free women to experience this complication. This risk is reduced if the woman discontinues cocaine use in the first trimester of pregnancy.

Drugs such as cocaine, alcohol, heroin, marijuana, crack, and PCP--all of which can cross the placental barrier--can cause profound, potentially irreversible damage in the newborn. Past research has shown that retarded fetal growth, premature delivery, low birth weight, Sudden Infant Death Syndrome, and drug-specific neonatal withdrawal syndromes are only a few of the pathological conditions associated with drug abuse by the mother. Many drug-exposed infants are difficult to care for during their first few months of life. Given the recent epidemic of drug abuse among pregnant women, information is now, and only slowly, becoming available on the far-reaching effects drug use during pregnancy appears to have on children born to drug-using women. Longitudinal studies designed to follow these children as they develop now is underway. Early findings indicate that the children tend to run increased risk of learning disabilities, and delayed motor, speech, and language development.

In response to the growing crisis of substance abusing women and children born addicted, the OSAP initiated a program in FY 1989 designed to develop innovative models of education, prevention and/or treatment for substance abusing pregnant women and their infants. Emphasis is placed on low-income pregnant and post-partum women and their infants. Projects are intended to promote

the involvement and coordinated participation of multiple organizations in delivering comprehensive services for substance using pregnant and post-partum women and their infants as well as increase the availability and accessibility of services to these populations. The goal of the projects is a decrease in the use of drug and alcohol abuse along with a corresponding increase in the proportion of healthy births.

ALCOHOL, DRUG ABUSE AND MENTAL HEALTH ADMINISTRATION

National of Alcohol and Alcohol Abuse

Infant Mortality Research: Fetal Alcohol Syndrome

Research has firmly established that alcohol consumption during pregnancy can cause birth defects. The severity of the defects is dose dependent, ranging from the extensive impairments associated with fetal alcohol syndrome (FAS) when drinking is heavy, to subtle behavioral and cognitive deficits at lower consumption levels. The incidence of FAS is frequently estimated at 1 to 3 cases per 1,000 live births; this translates into 3,600 to 10,000 new cases in the United States per year. THus, FAS is one of the leading known causes of mental retardation. The incidence of partial manifestations of the syndrome (called fetal alcohol effects, or FAE) is estimated to be about three times greater.

The persistence of alcohol-induced birth defects is an area of major concern. In a recent follow-up study, FAS children were examined at various times after their original diagnosis. While significant improvements were found in some of the defining features such as craniofacial disfigurement, cognitive deficiencies were remarkably persistent.

Recent evidence indicates that risk for giving birth to FAS infants may be modified by other factors, including genetics and maternal variables. For example, epidemiological studies have demonstrated that blacks have greater susceptibility to the harmful effects of prenatal alcohol exposure. And while research continues to identify factors that may modify the risk of alcohol-related birth defects, cross-cultural studies demonstrate that that no races or ethnic groups are immune. Researchers are working to improve identification of pregnant women who are at risk of continuing alcohol abuse. Recent studies indicate that the best predictors of continued drinking throughout pregnancy are the length of drinking history, tolerance to alcohol, and a history of alcohol-related illness.

An important area of study is the role of alcohol as a cofactor in the transmission of HIV/AIDS from the mother to the fetus. Recent findings indicate that maternal alcohol consumption has a profound effect on the development of the fetal immune system. Ethanol inhibits transport of antibodies across the placenta, suppresses proliferation and maturation of thymocytes, and decreases the offsprings' ability to resist infections. The latter effect has been shown for paternal alcohol consumption as well. Further research in this area is needed.

The effects of low-level or moderate drinking on prenatal development are of considerable concern because this pattern of drinking is so prevalent. The Institute continues to support

three longitudinal studies of the relationship between maternal alcohol consumption during pregnancy and developmental outcomes in offspring. Subtle neurobehavioral effects have been observed at ages 4 and 7 in a large group of children who have been followed since birth and whose mothers drank moderately during pregnancy.

The Institute continues to fund a number of laboratory studies of alcohol's effects on pre- and postnatal development. In recent years, studies to determine why and how alcohol adversely affects the fetus have uncovered a number of mechanisms that likely contribute in differing degrees to FAS. These include alcohol-induced placental dysfunction, direct alcohol and acetaldehyde toxicity, fetal hypoxia, and the role of potent, naturally occurring hormone-like substances called prostaglandins. Continued research is required to answer a number of pressing questions: What is the minimal dose of alcohol which portends a risk to the fetus? Are there therapeutic interventions which can aid recovery from injury? and What are the most effective ways to minimize alcohol use during pregnancy? This last question is particularly pertinent early in the first trimester, a critical period for birth defects, when a woman may not yet be aware of her pregnancy.

ALCOHOL, DRUG ABUSE AND MENTAL HEALTH ADMINISTRATION

Office for Treatment Improvement

Infant Mortality

The Office for Treatment Improvement (OTI) provides support to infant mortality programs through OTI categorical grants and the ADMS Block Grants. In FY 1991 OTI will make approximately $17.6 million available to treatment programs for pregnant women and their children. This is approximately 16% of the total amount allocated to OTI for the categorical grants (Treatment Improvement Grants and Grants to Crisis Areas). In addition, approximately 15% of OTI's ADMS Block Grant funds ($211.3 million) will be available to states for treatment programs aimed at pregnant women and their children.

AGENCY FOR HEALTH CARE POLICY AND RESEARCH

Formerly the
National Center for Health Services Research
and Health Care Technology Assessment

INFANT MORTALITY

The Agency for Health Care Policy and Research (AHCPR) was established on December 19, 1989 as a separate Public Health Service (PHS) agency by the Omnibus Budget Reconciliation Act of 1989, P.L. 101-239. As authorized under a new Title IX of the PHS Act, the purpose of the agency is to enhance the quality, appropriateness, and effectiveness of health care services and to improve access to such services. This will be accomplished through the establishment of a broad base of scientific research and through the promotion of improvements in clinical practice and in the organization, financing, and delivery of health care services. The new agency replaces the former National Center for Health Services Research and Health Care Technology Assessment.

As the leader of Federal efforts in outcomes research and health services research, the AHCPR seeks to create and disseminate new knowledge and better understanding of the processes by which health services are made available and how they may be provided more efficiently and effectively. The AHCPR conducts and supports scientific research that tests the assumptions on which current health policies and practices are based, assesses the performance of the health care system, and examines alternate ways to organize, finance, and deliver health services. AHCPR's program is directed towards the needs of health care policymakers, providers, and consumers. It addresses the full array of health care issues, among them infant mortality.

In recent years, increased attention has been focused at the Federal, State, and local level on the health problems faced by American's children. The reasons for this increased attention are many, and include the following factors:

- The United States not only continues to compare unfavorably with other developed countries in such important measures of child health status as infant mortality, but in certain states and localities, infant mortality rates exceed those of some developing countries.

- Earlier trends showing improvements in a number of important U.S. health status indicators, such as the proportion of babies born with low birthweight, have flattened out, showing little or no improvement during the 1980's.

- Changes in the health care marketplace have left an increasing number of children without any form of private or public health care insurance. The combination of rising

malpractice insurance premiums and low payment levels has left many low-income pregnant women, even those covered by Medicaid, without access to adequate prenatal care, while some with access do not avail themselves of it.

In spite of these problems, health services research has been able to identify interventions that are not only effective in addressing certain child health problems, but certain of these have also been shown to reduce future health care costs associated with these problems. Health services research has also helped identify those factors that enhance or hinder the successful implementation of these interventions.

Given the very significant roles that State and local governments historically have played with respect to child health, particularly for low-income children, the above developments in many cases have necessitated a new look at the child health programs and policies that these entities have established. Indeed, as health services research findings -- including assessments of the experiences of States and localities operating innovative programs -- identify those strategies and interventions that hold the greatest promise for improving child health status, it may be appropriate for individual jurisdictions to rethink and perhaps reorganize their existing activities.

User Liaison Program

The Agency's User Liaison Program developed and sponsored on October 3-6, 1989, a workshop for State and local officials entitled, "Designing, Implementing and Financing Health Services for Children." The purpose of the workshop was to provide senior State legislative and executive branch officials, as well as county and local officials, with an in-depth look at health services research and related information that will allow them to make more informed decisions concerning child health activities carried out within their jurisdictions. This workshop was designed for senior State and local government officials from both the legislative and executive branches who have major responsibilities for policymaking that affects the planning, regulation, financing, delivery and evaluation of health services. It was not intended for officials with specific responsibility for the day-to-day management and operation of child health programs and services, but rather for senior policymakers with broad responsibilities for a range of issues, including child health and welfare.

Through this three-day workshop, State and local officials were provided with an opportunity to:

- gain a fuller understanding of the nature of the major health problems affecting children, as well as the principal factors which affect child health and survival;

- review the principal roles and responsibilities that State and local government play with respect to child health and examine the major programs and policies these jurisdiction use to carry out these responsibilities;

- discuss recent changes in the public and private organization and financing of children's health services and explore their implications for the development of new initiatives at the State and local levels;

- examine available health services research that identifies opportunities for the development of new programs and policies that can have a positive effect on the health of children as well as those findings which identify approaches that have failed;

- examine different operational approaches and strategies that individual States or localities have found to be effective in meeting the goals of promoting the health of children in varying settings and across differing age groups;

- explore strategies which may be used at the State and local level for the evaluation of child health initiatives.

The Workshop included a session entitled, "Strategies to Address Child Health Problems: Pregnancy and Infancy." This session focused on the major health problems of infancy (the first year of life). Because of the profound and long-term impact of a mother's pre-natal experience on the health of her infant, this session also explored in depth the options and opportunities for the promotion of infant health through prenatal policies and programs. The discussion focused on low-birthweight, infant mortality and factors associated with them. Strategies examined included the provision of adequate prenatal care as well as State and local approaches that have been used to overcome a number of significant obstacles encountered in expanding prenatal care services, namely:

- difficulty in establishing, operating and funding prenatal care programs and facilitating their maximum utilization;

- lack of coordination of service delivery across different public programs;

- an unwillingness of a significant number of physicians to provide prenatal and delivery services to low-income women because of malpractice/liability or reimbursement concerns; and

- difficulties in establishing and maintaining low-income pregnant women's participation in prenatal care programs.

The discussion of these strategies included an examination of the evidence which exists concerning their effectiveness and costs.

Extramural Research

In the past, infant mortality has not been a separate topic area at NCHSR (now AHCPR). However, a number of projects have been funded under other subjects such as health care and the disadvantaged, rural health care, primary care and nursing services research.

Projects Completed in Fiscal Year 1989:

"The Effect of WIC on Adolescent Pregnancy Outcomes"
Gail D. Pearson, M.B.A., Johns Hopkins University, Grant No. HS05970

This dissertation research sought to examine the effect of the WIC (the Federal special supplemental food program for Women, Infants, and Children) program availability in large U.S. counties on birthweight, gestational age, and timely prenatal care use among pregnant adolescents during the years 1975 through 1984. Using the household health production model as the theoretical framework, collected data were analyzed through a series of regression equations. The sampling frame involved counties which had a white population of at least 10,000 or a black population of at least 5,000 according to the 1980 census.

This study found no significant effects of WIC program availability on birthweight, preterm delivery, or the use of prenatal car among adolescents. Participation of adolescents in WIC, however, was not assessed directly in this study. Several possible explanations for these findings are discussed. The findings may reflect the low participation rates in WIC programs by pregnant adolescents even though the guidelines governing WIC eligibility and participation gives priority to pregnant adolescents.

New Starts in Fiscal Year 1989:

"Use of Perinatal/Infant Services by Hispanics in AHCCS"
Patricia D. Moore, Ph.D., Arizona State University, Grant No. HS06127

Mexican-Americans have been shown to have lower use rates of prenatal care and well baby care, even when financial and providers barriers have been lowered. This study will evaluate the effects of acculturation, family function, and past experience on the utilization of

preventive services for a group of Mexican-Americans and whites enrolled in the Arizona state Medicaid HMO called AHCCS. Results are expected to assist in designing more effective health care delivery system for this rapidly expanding population of Americans.

"Practice Variations in Prenatal and Intraparatum Care"
Roger A. Rosenblatt, M.D., University of Washington, Grant No. HS06166

This study will explore the relationship between variations in prenatal care received by low risk women in Washington state to provider type (obstetrician, family practitioner, nurse practitioner), location (urban/rural), practice organization and hospital setting. Outcomes to be collected include perinatal mortality, morbidity, and charges. The results will assist in decisions regarding appropriate utilization of prenatal technology for low risk women.

Projects Ongoing in FY 1989:

"The Adequacy and Effectiveness of Prenatal Care"
Mary Jo Hansell, University of California at Los Angeles, Grant No. HS06105

This study will attempt to identify the particular elements in programs of prenatal care which are most clearly associated with lower infant mortality rates. Data to be used are from the 1980 National Natality Survey (NNS), the 1980 National Fetal Mortality Survey (NFMS) and the 1980 American Hospital Association Survey (AHAS). The NNS, based on a random sample of 9,941 live births, and the NFMS, based on a random sample of 6,386 late (>28 weeks) fetal births, contain data on the mothers' risk factors (medical and behavioral histories and sociodemographic variables) and pregnancy outcomes. Respondents were married mothers only, physicians who provided prenatal and intrapartum care, and hospital staff where deliveries occurred. The AHAS contains data on each hospital's obstetric facilities, educational affiliation and accreditation.

"Low Birthweight and the Quality/Content of Prenatal Care"
Diane B. Petitti, M.D., Kaiser Foundation Research Institute, Grant No. HS06031

Under the direction of Dr. Petitti this study will examine the association of low birthweight with the earliness, adequacy, quality, and content of prenatal care. This is a retrospective study which will test the hypotheses that the risk from low birthweight is reduced in pregnant

women who receive adequate and early prenatal care, receive a screen for bacteriuria and receive assessment and counseling about smoking and substance abuse in pregnancy.

"Physiologic Severity Index for Neonatal Intensive Care"
Douglas K. Richardson, M.D., Brigham and Women's Hospital, Grant No. HS06123

Dr. Richardson is carrying out a study to develop a severity of illness index for neonatal intensive care units (NICUs) to permit accurate comparative studies of NICU care between hospitals, across regions and over time. While there are physiologic severity measures for adult and pediatric intensive care areas, no such measures exist for neonatal intensive care units. The issue of neonatal care and variation in treatment is particularly timely considering the current neonatal mortality rates. The research findings will identify whether the severity of index tool provides better explanatory power of neonatal outcomes than the traditional measures of birthweight and Apgar score. This tool will be valuable in assessing variation in neonatal outcomes across hospital settings.

"Mediators of Birth Outcomes Among Three Low-Income Ethnic Groups"
Ruth E. Zambrana, University of California at Los Angeles, Grant No. HS05518

Dr. Zambrana is examining the ethnic differences in birth outcomes among primiparous, low-income Black, Mexican-American and Mexican immigrant women who receive their prenatal care from providers in community health centers and primary care centers in public/private hospitals in Los Angeles, California. The study is designed to determine if observed differences in medical risks contribute to differences in birth outcomes, if prenatal care influences neonatal outcomes when medical risk is controlled, if stress and anxiety contribute to birth outcomes, and if the three groups differ in the social support they receive during pregnancy.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

INFANT MORTALITY

In the next decade, more than 400,000 U.S. children will die before their first birthday. Many are born too small or too soon to survive, while others die within the first year because of birth defects or sudden infant death syndrome (SIDS).

The infant mortality rate, which is the number of deaths of children under one year of age per 1,000 live births in a given year, dropped dramatically in the United States from 21.8 in 1968 to 10.1 per 1000 live births in 1987. However, the decline in the U.S. mortality rate leveled off in the early 1980s and has improved only from 10.4 per 1,000 in 1986 to 9.9 in 1987.

A comparison of the latest U.S. infant mortality rate to 17 other nations reveals that more than a dozen countries continue to have lower infant mortality rates than ours. Among those nations with lower provisional rates in 1988 were Hong Kong and Singapore, with 7.4 and 7.0 deaths per 1,000 live births respectively, Sweden with 5.58, and Japan with 4.8 deaths per 1,000. Although many sources think that the absence of a uniform international reporting system may contribute to the poor U.S. ranking, the inability to eliminate infant mortality is paradoxical for a nation that spends billions of dollars each year on scientific research and medical care and whose hospitals and neonatal intensive care units rank among the best in the world. Advances in medical technology have succeeded in saving increasing numbers of undersized, critically-ill newborns and have played a role in containing the nation's infant mortality rate. However, it is clear that the large number of low birth weight infants born in the U.S. is a major contributor to our high infant mortality rate. Infants who weigh less than 5 pounds 8 ounces (low birth weight) account for approximately 7 percent of all U.S. births but represent 60 percent of deaths occurring during the first year of life. Approximately 45 percent of the low-birth-weight deaths are associated with congenital anomalies.

Because they represent such a large proportion of the infant morality rate, any change in the incidence or survival rate of low birth weight infants will influence the infant mortality rate. The incidence of low birth weight actually increased from 6.8 percent in 1986 to 6.9 percent in 1987, which represents the highest level of low birth weight observed since 1979 when it was also 6.9 percent. This represents a worrisome deviation from recent trends: between 1970 and 1981 the low-birth-weight rate declined 1.3 percent per year and then remained fairly constant from 1981 until 1986.

There appears to be no single reason for the disproportionally high number of low-birth-weight babies born in the United States. Risk factors identified include younger and older maternal age; high parity; a poor reproductive history, especially a history of low birth weight spanning generations; low level of socioeconomic status and education; poor or no prenatal care; and smoking and substance abuse.

In many instances, pregnant women in high-risk groups--particularly poor, urban, black women--fail to get early, comprehensive prenatal care that includes screening for such potentially harmful conditions as nutritional deficiencies, smoking, alcohol or drug abuse. Early intervention to improve nutrition and reverse such social habits can reduce the chances of a low-birth-weight baby.

However, all low-birth-weight infants are not the product of high-risk pregnancies. Healthy women with good nutrition and prenatal care and no harmful social habits also deliver early because of premature labor or deliver infants who are undersized because of interuterine growth retardation. Researchers are investigating the basic biological reasons for low birth weight in such babies, as well as the explanation for such major causes of infant mortality as infectious diseases, birth defects, and SIDS.

The National Institute of Child Health and Human Development (NICHD) is the leader in the infant mortality research effort for the National Institutes of Health (NIH). Other NIH institutes that conduct or support studies related to infant mortality include the National Heart, Lung and Blood Institute (NHLBI); the National Institute of Neurological Disorders and Stroke (NINDS); the National Institute of Allergy and Infectious Diseases (NIAID); the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS); the Division of Research Resources (DRR); and the National Center for Nursing Research (NCNR).

Since its inception in 1962, NICHD has sponsored studies that have helped the medical community improve the survival rates for all infants. Research efforts accelerated in 1985 with the Institute's Infant Mortality/Low Birth Weight Initiative, which encompasses many studies. The goal of each of these studies is to gain knowledge relating to the causes and prevention of infant mortality.

NICHD epidemiologists, statisticians and demographers are conducting and monitoring numerous studies designed to explore the infant mortality problem. One of their major research thrusts has been to make accurate comparisons of infant death rates among different countries, including Australia, European countries and Japan. As part of this effort, an NICHD statistical team headed by Howard J. Hoffman found significant differences among five racial and national groups examined. In comparing infant mortality rates attributable to intrauterine

growth retardation (IUGR) in U.S. blacks, U.S. whites, Aborigines, Australian whites, and Japanese, the team concluded that individual growth standards must be developed for each group.

Another multinational study explored the birth weight-specific trends in perinatal and infant mortality from 1972 to 1985. This study suggested that differences in the incidence of multiple births may contribute to the high U.S. infant mortality rate. The incidence of multiple births ranged from a low of 1.25 percent of births in Japan to about 2 percent of births in Norway, Scotland, Sweden, and among U.S. whites, to almost 2.5 percent of births to U.S. blacks. Multiple births account for a relatively higher percent of perinatal or infant deaths in all countries. Sweden has the fewest (5 percent) and the U.S. and Scotland the highest (10 to 11 percent) of deaths among multiple births.

A number of studies hope to define the contribution of lifestyles and ethnic differences to infant mortality. Lifestyles of U.S. white, black, Mexican, Chinese and Puerto Rican women will be compared to try to determine why Mexican-American infants are significantly bigger than black infants (and therefore have a better chance of survival), despite the fact that women in both ethnic groups share known risk factors associated with low income, limited education, and inadequate nutrition and prenatal care. Because black women in the U.S. have twice the risk of delivering a low-birth-weight infant as white or Hispanic women with comparable backgrounds, in addition to the known risk factors associated with low birth weight, another study will look at such factors as social support, level of physical activity, stress, and attitudes and beliefs about pregnancy. The NICHD-supported study is headed by Dr. Patricia Shiono and is conducted in prenatal clinics affiliated with Columbia University in New York City and Northwestern University in Chicago, Illinois.

Low Birth Weight

As noted above, low-birth-weight infants account for a large proportion of newborn deaths and the number of these low-birth-weight infants is increasing. Accordingly, NICHD supports more than 100 research projects on high-risk pregnancy, with the goal of increasing our understanding of why some babies are born prematurely and what factors initiate labor. Researchers are investigating the causes of premature birth and intrauterine growth retardation, both of which result in low birth weight. Through the studies, scientists hope to learn not only how they can improve the survival chances of low-birth-weight babies through further neonatal intensive care advances, but also how they can prevent low birth weight.

Improvements in Survival

The development of sophisticated, life-saving equipment in neonatal intensive care units in hospitals throughout the United States is largely responsible for the decline in newborn deaths and the infant mortality rate. Since 1960, advancing technology has dramatically reduced the number of deaths during the first 28 days of life. For babies with very low birth weight--infants who weight less than 3 pounds, 5 ounces at birth--survival rates improved from 28 percent in 1960 to 73 percent in the early 1980s. The latest data from the NICHD Neonatal Intensive Care Unit Research Network reveal that 90 percent of infants born at weights between 2 pounds 3 ounces and 3 pounds 5 ounces survive; however, only 33 percent of infants born weighing less than 1 pound 10 ounces survive. The NICHD has funded many of the life-saving technological advances that have been developed for newborns over the past 25 years. The research has led to better intravenous nutrient regimens and improved treatments for such life-threatening conditions as respiratory distress syndrome and intracranial hemorrhage, as well as various infections.

Neonatal Intensive Care Network

In 1985, NICHD formed a research network of Neonatal Intensive Care Units (NICUs) in seven university hospitals across the country. The centers, which perform large clinical trials, provide NICHD with a faster, more effective system of evaluating neonatal intensive care treatments. The NICU network is collaborating on several ongoing studies, including studies designed to document the morbidity, mortality, and requirements for care for infants with a birth weight less than 3 pounds 5 ounces. Other studies include a clinical trial to determine the effectiveness of intravenous immunoglobulin in the prevention of infection in low-birth-weight infants. More than 2,500 infants weighing less than 3 pounds, 5 ounces are included in this multi-year research project whose results will be reported next year.

The use of surfactant therapy in the prevention and treatment of respiratory distress syndrome is also under study in the NICU Network. Neonatal respiratory distress syndrome (RDS) affects 40,000 infants born in the United States each year and results in the deaths of 5,000. It is caused by the inability of the lungs of premature infants to make surfactant, a material that helps the lungs inflate easily and prevents their collapse during expiration. Surfactant is produced in the lungs of a fetus in the last trimester. Previous small studies using a variety of different surfactants and treatment regimens have documented that surfactant therapy can reduce the severity of respiratory distress syndrome and lead to a decrease in both mortality and morbidity of premature infants. In anticipation of the introduction of surfactant into routine care, the NICU network is currently studying the effectiveness of surfactant therapy to determine whether it is associated with a decrease in

the mortality rate and length of time of infants weighing 1 pound 5 ounces to 2 pounds 14 ounces at birth must spend linked to mechanical ventilation. Two surfactant preparations will be available before the end of the year under FDA-approved treatment regimens. The NICU Network will perform a large, multi-center, randomized, blinded clinical trial of the two surfactants in 1990.

Maternal-Fetal Medicine Research Network

A network of Maternal-Fetal Medicine Units (MFMUs) was also funded in 1985 to perform clinical trials designed to evaluate maternal-fetal treatments. The MFMU network is conducting a clinical trial to determine whether low-dose aspirin can prevent preeclampsia (pregnancy-induced hypertension) in women pregnant with their first child. The first 600 of the 3,000 women to be studied were enrolled in 1989. Safety studies will be conducted throughout the trial to ensure that there are no adverse effects on either the mother or the unborn child. Ancillary studies will look for biomarkers that can help scientists identify which women are likely to develop preeclampsia.

The MFMU network is also conducting a clinical trial to determine if antibiotics can enhance the effect of tocolytic medications used to arrest preterm labor. Women are taking low doses of standard antibiotics during pregnancy to determine their value in preventing preterm labor. An ancillary study will attempt to prove that infection is present by testing amniotic fluids. One hypothesis is that the body's reaction to bacteria in the amniotic fluid alters the production of enzymes that trigger preterm labor. This 24-month study of 700 pregnant women began in December 1989.

The Use of Drugs in the NICU

NICHD is also sponsoring research on medication use and adverse reactions in NICUs. Dr. Allen A. Mitchell at Boston University in Massachusetts heads a team of researchers studying the use of morphine sulfate as a sedative during medical and surgical procedures. Morphine sulfate use increased 2 percent in 1975 to 24 percent in 1985, with a six-fold increase in use in recent years. Eleven percent of the newborns who received the drug had adverse reactions. Trichloromethane, an organic solvent which is used to remove adhesive tape from infant skin, is also under study. Because the drug has documented toxicity in cases of occupational exposure, research is focusing on absorption through permeable infant skin. Finally, the pharmacokinetics of tolazoline, a potent vasodilator used in the treatment of pulmonary hypertension, is being investigated in the NICU Network.

Nutrient Requirements of Low-Birth-Weight Infants

NICHD supports research directed toward the nutritional needs of premature and intrauterine-growth-retarded infants. These studies are designed to provide a scientific basis for the provision of optimal nutrition to these tiny infants whose survival depends on nutrition and growth. The metabolic and absorptive capabilities of low-birth-weight babies differ from full-term babies; therefore nutritional strategies must be tailored to meet their unique nutritional requirements. Investigators are searching to define specific diets by which nutritional deficiencies can be prevented or treated in these infants.

In Washington, D.C., Dr. Cecile Edwards and her colleagues at Howard University Hospital and D.C. General Hospital are studying the role of nutrition in low-birth-weight infants born to urban blacks. The incidence of low birth weight births among blacks is 12.5 percent, compared to 5.7 percent for whites. In the nation's capital, 18 percent of black babies are low birth weight; 20.6 percent of births at the Howard University Hospital weigh less than 5 pounds, 8 ounces.

Women in the Edwards' study were from 16 to 35 years of age and were enrolled before the 26th week of their first pregnancy. Eighty-five percent were unmarried. Twenty percent of the women in the study group failed to gain the recommended minimum weight during pregnancy and had serious nutritional deficiencies, reflected in subnormal serum ferritin and folate levels. Maternal prepregnancy weight, maximum maternal weight gain during pregnancy, and weekly weight gain and folate intake during the second trimester were significantly correlated with birth weight. Women who completed the program had significantly larger infants compared to control infants (low-birth-weight incidence of 8.9 vs. 20 percent).

In another study of nutrition for low-birth-weight infants, Dr. Margit Hamosh and her colleagues at Georgetown University in Washington, D.C., continue a multi-year project to assess fatty acids as an energy source. This group has done extensive work on medium-chain triglycerides, which can be more readily absorbed, in the diet of low birth weight infants. Studies now in progress will continue to evaluate the contribution of gastric enzymes to fat digestion and the use of enzyme activity levels in gastric mucosa to diagnose stomach disorders.

Intrauterine Growth Retardation

Infants who have experienced inadequate growth in utero at any stage of gestation are termed growth retarded. Term infants with intrauterine growth retardation (IUGR) usually weigh less than 5 pounds, 8 ounces when they are born. Like the low-birth-weight infants, newborns with IUGR are at a higher risk of dying

before their first birthday than are full-term babies of normal birth weight. NICHD studies of these babies examine biological, epidemiologic, behavioral and social factors related to IUGR, as well as treatment methods.

Researchers at NICHD have also noted differences in growth of black versus white fetuses in an ultrasound study of growth retardation in Alabama. Ultrasound measurements during the second and third trimesters of pregnancy revealed differences in fetal growth related to sex and race. Male infants of both races had larger head and abdominal circumferences than females. Black infants had longer femur lengths than whites at each gestational week examined. Since black infants also were found to have shorter crown-heel lengths at birth, after adjusting for gestational age at delivery, it is possible that the observed difference in body length proportions (longer legs and shorter trunks in black infants than white) is an important factor in understanding the birth weight differences between black and white infants.

Dr. Daniel Edelstone at the University of Pittsburgh is investigating the hypothesis that maternal anemia affects the oxygen supply to the fetus and thus influence its growth. His research suggests that anemia early in pregnancy leads to compensations that enable the fetus to maintain normal oxygenation and growth. When anemia is late in gestation or exceeds the capacity of compensatory mechanisms, the amount of oxygen reaching the fetus is reduced.

The role of fetal growth factors and their relationship to IUGR are being studied by a team of scientists led by Dr. Joseph D'Ercole at the University of North Carolina in Chapel Hill. Using a rat intrauterine model, this group is trying to determine whether fetal growth retardation associated with maternal malnutrition is mediated by a reduction in insulin-like growth factors (IGFs). Preliminary analysis of the study in which the pregnant rat is fasted from day 18-21 suggests that both mothers and fetuses are resistant to fasting and that their growth factors do not drop dramatically as in non-pregnant animals.

Researchers in the institute's Prevention Research Program are conducting studies to help determine whether certain groups of women are at risk of having a baby with IUGR. Staff scientist Dr. Mark Klebanoff and his colleagues are looking at intergenerational links to low-birth-weight babies. Using matched maternal-infant birth certificates in Tennessee, they found that mothers who themselves were low-birth-weight babies were four times more likely to have babies with IUGR, but only 1.6 times as likely to have a preterm baby. Similar patterns occurred in very large studies performed in Sweden and Denmark in collaboration with the World Health Organization. Low-birth-weight patterns between generations are also being studied in research projects in Philadelphia and Providence.

Women who were themselves low-birth-weight babies may require careful monitoring during pregnancy for signs of preterm labor or IUGR. These findings alert the pediatrician to inquire about the mother's weight at birth when a small but otherwise normal-appearing infant has been delivered. The inter-generational link may provide another explanation for difficulty in reducing the incidence of low-birth-weight babies.

Behavioral and Social Risk Factors in Low Birth Weight

A large NICHD study of mothers of low-birth-weight infants has produced preliminary data to support mounting evidence that such adverse health habits as smoking, drinking and illegal drug use pose a major risk factor for low-birth-weight infants. Socioeconomic variables including housing, level of education and environment also were shown to play a role in low birth weight. Researchers headed by Dr. Heinz Berendes, director of the institute's Prevention Research Program, studied the influence of social and behavioral characteristics on the risk of having a low-birth-weight baby. A striking 50 percent of more than 1,000 women who delivered babies in six Washington, D.C., hospitals had low-birth-weight infants. Preliminary analyses indicate that the combined effects of smoking, drinking and illegal drug use account for about 40 percent of the low-birth-weight babies born to this group of inner-city women. Drug abuse alone is responsible for 20 percent of the low-birth-weight risk in this group.

A NICHD-funded study by Dr. Mary Sexton and collaborators at the University of Maryland demonstrated that smoking cessation as late as the third trimester of pregnancy can significantly ameliorate the fetal growth retardation associated with smoking; however, she noted that such behavior change was difficult to bring about. A study completed earlier this year adds disturbing evidence that smoking during pregnancy is the most important single risk factor for low birth weight that could be eliminated by behavior modification. The study of 1,000 black women in the District of Columbia showed that smoking alone accounted for 34 percent of low birth weight. The other factors found to be associated with low birth weight were use of "street drugs", alcohol, and a history of a low-birth-weight or stillborn child. Of the participants--500 cases of low-birth-weight and an equal control group--47 percent were between the ages of 18 and 24; 43 percent had less than a 12th grade education; more than 70 percent had never been married; and 50 percent were below the poverty line. NICHD staff member Leslie Cooper is now working with members of the American College of Obstetricians and Gynecologists and scientists at the National Cancer Institute, National Heart, Lung and Blood Institute, and the Centers for Disease Control to develop a pilot intervention program to help women stop smoking during pregnancy.

Another intervention program, the Better Babies Project in the District of Columbia, is attempting to reduce the incidence of low birth weight by identifying pregnant women in the high-risk areas and intervening with health education and social services. The program attempts to help pregnant women change patterns of smoking, alcohol and drug abuse as part of prenatal care. Some data already suggest that most women can have a normal baby if drugs, for example, are removed early in the pregnancy.

In another study in the Prevention Research Program, Howard J. Hoffman of NICHD, Dr. Robert Goldenburg of the University of Alabama, and colleagues are comparing risk factors for fetal growth retardation in Norwegian and Alabama women with common risk factors of smoking and a previous low-birth-weight infant. They found that women with lower educational levels, poor housing, no access to a car, strenuous physical activity, and high levels of depression, anxiety and stress had higher rates of IUGR births.

The impact of work-related stress on pregnancy is being studied in a project to evaluate medical residents and their spouses. The study, which began in September 1989, will compare the pregnancy outcome of 5,000 female medical school graduates with the non-physician wives of 5,000 male classmates. The study provides the unusual opportunity to evaluate stress without the confounding variables of poverty, low educational levels, and poor environment often found among women considered high risk candidates for low-birth-weight babies.

Prenatal Care

In 1986 an expert panel, appointed by the PHS Committee on Low Birth Weight Prevention, was charged with recommending how much and what types of prenatal care are needed. The NICHD served as the coordinator of this effort. After an extensive study of various aspects of prenatal care, the panel's recommendations were published in a report issued by the U.S. Public Health Service in October 1989. The panel reaffirmed prenatal care as the foundation for improved health of the pregnant woman, the infant, and the family. However, it concluded that ideally care should begin prior to conception, and that every effort should be made to include both the man and the woman in this preconceptional counseling. In order to enable every woman and her family to benefit from the biological and technological advances that have been made, the panel concluded that care should be expanded to include medical and family follow-up up to a year after the child is born. Multi-disciplinary health care teams were not only charged with providing earlier and longer prenatal care, with expanded content, but they were urged to take new approaches to prenatal care delivery.

The panel called for a shift in emphasis from healthy to at-risk expectant mothers. It suggested that many routine tests and procedures are expensive and unnecessary, but it cautioned that routine care must continue to provide health care practitioners the opportunity to monitor patients for development of risk factors during the pregnancy.

The experts identified early and continuing risk assessment, health promotion, and medical and psychosocial intervention and follow-up as the three basic components of prenatal care. Care for all pregnancies should include a complete medical history, education and counseling in healthy behavior and parenting, and treatment of any existing illnesses. Beginning with preconception care, the goals of the panel extended from reduction of preterm births, intrauterine growth retardation, congenital anomalies and failure to thrive, to promoting healthy growth and development, immunization, and health care supervision of the child. Although the panel was aware of the implications for prenatal care providers, government agencies, institutions and third-party payers, it did not suggest a change in the basic relationship between the woman and her prenatal care provider. The report urged public and private organizations and agencies to support badly needed research and studies in several areas, in addition to emphasizing the importance of making care available to all women regardless of economic status.

Sudden Infant Death Syndrome

NICHD has a long-standing commitment to research on sudden infant death syndrome (SIDS), commonly known as crib death. SIDS is defined as a sudden, unexpected death that is unexplained after a complete postmortem investigation. SIDS is the leading cause of death in American children between 1 and 12 months of age and is responsible for 7,000 deaths annually. Most of the deaths occur quietly, apparently during sleep. The exact causes of SIDS are still unknown, but scientists appear to have eliminated choking, parental neglect, common infection, and allergy.

Because of the critical need for research, the NICHD SIDS Cooperative Epidemiologic Study was initiated in 1978 to find out how SIDS infants are different from other babies. In a report published in 1987 after a decade of study, 90 percent of SIDS infants were noted to die before they were 6 months old, and 98 percent died before they were a year old. The peak times of death are between midnight and 8 a.m., and more deaths occur during cold weather months. Black infants are nearly three times as likely to die of SIDS as white infants, and babies born to smokers or teenagers, siblings of SIDS victims, or premature or low-birth-weight infants are at higher risk.

The SIDS Histopathology Atlas is expected to be published next year through the Armed Forces Institute of Pathology. It will summarize the findings comparing the 757 singleton SIDS cases and 65 explained death cases which were reviewed by a panel of three SIDS pathologists in the NICHD SIDS Cooperative Epidemiological Study. Eligibility for the extensive study was based on SIDS victims who died between October 1978 through December 1979 in six geographical areas. Two sets of living controls were matched by age to the SIDS cases, with one control group being matched by race (black vs. non-black) and low birth weight. Among the panel's histological findings were pinpoint hemorrhages in the thoracic cavity which were observed significantly more often among SIDS cases compared to explained deaths. Among explained deaths compared to SIDS deaths, there was an increased incidence of fatty changes in the liver and a higher incidence of inflammation of the trachea.

Dr. Ronald M. Harper at the University of California in Los Angeles, has compared the heart rates of infants who later died of SIDS with other infants the same age. SIDS infants were found to have a higher heart rate and decreased heart rate variability. Further analysis revealed that SIDS babies have altered coordination between cardiac and breathing mechanisms. These results support the concept that SIDS infants have immature cardiorespiratory control mechanisms.

The recipient of one of the eight new SIDS research grants awarded this year, Dr. Harper will investigate the organization and physiological measures that define sleep states in normal infants and two groups of at-risk SIDS infants - those who later died of SIDS and siblings of SIDS victims. The project will examine whether SIDS victims die from a failure of mechanisms that normally allow transitions from one sleep state to another and the physiologic signs measured during different sleep states.

In an ongoing study of autopsies, Dr. Charles R. Roe, an NICHD grantee at Duke University Medical Center in Durham, North Carolina, is looking for evidence of abnormal fat metabolism in SIDS victims. A new study beginning this year is examining the role of inherited metabolic disorders as a cause of sudden death in infants. Researchers are looking for abnormal metabolites in infants at risk for SIDS using sophisticated screening technology. The goal is to identify new inherited enzyme defects. These types of genetic defects could be important for neonatal and prenatal screening and nutritional intervention in the future to prevent disease and death. Although only a small fraction of infants is affected, the possibility of prevention and treatment is very high.

Dr. William E. Cameron at the University of Pittsburgh School of Medicine and Dr. Gabriel G. Haddad at Yale University are doing similar studies of respiratory maturation in animals as models for human infant development. Dr. Cameron is examining the development of neural control of the upper airway muscles

with that of the diaphragm during postnatal development, in order to define the role of the motor neurons in shaping breathing patterns. Dr. Haddad's project will investigate the cellular and molecular response to hypoxia in the central nervous system, specifically the brain stem.

Extensive study continues to provide better understanding of the cause, effect, and consequences of abnormal breathing patterns in newborns, the role of mechanisms that arouse infants from sleep, and the development of cardiorespiratory systems.

Birth Defects

More than 250,000 children are born each year with mental or physical disorders; thus birth defects continue to be a leading cause of death in all newborns. NICHD supports numerous research projects designed to identify problems in development and to identify specific genes responsible for birth defects. The projects include clinical and animal models of birth defects and biological research designed to understand normal development processes using molecular genetics and biochemistry.

Central nervous system defects common in newborns make up the largest proportion of potentially fatal birth defects. Spina bifida, one of the most prevalent birth defects, is one focus of the institute's basic research. This defect, in which the spinal canal fails to close completely, occurs in one to two babies in every 1,000 babies born in the United States; the complications claim the lives of 5 to 20 percent of those affected. NICHD-supported studies indicate that of those who do survive the first 24 hours after birth, 75 percent will have severe physical handicaps, while 20 percent will have moderate or severe mental retardation.

Neural tube defects, which include anencephaly and congenital hydrocephalus, are thought to have multifactorial genetic and environmental origins. Therefore, they are considered to result from interaction between a number of inherited genes and unidentified environmental factors. In response to the need for research models, two mouse models have been developed and are being distributed to scientists working in this area. The models--the curly tail mouse mutant and the T-curly tailed mutation--closely mimic spina bifida found in humans. NICHD-supported studies revealed that curly tail mouse spina bifida is due to a delay in the closure of the posterior end of the neural tube of the early embryo. NICHD recently sponsored a research conference on the etiology of spina bifida and other neural tube defects in which the current knowledge base was reviewed and a research agenda generated.

Research on the influence of periconceptional vitamin intake on the incidence of central nervous system disorders such as spina bifida has yielded conflicting results. In an NICHD study

of 1,700 pregnant women in California and Illinois between 1985 and 1987, it was found that vitamin use around the time of conception did not prevent neural tube defects. Other recent studies suggest that vitamins taken by the expectant mother before or shortly after she becomes pregnant protect the infant from neural tube defects. The results of the NICHD study may differ from these other studies because of methodology. For example, the amount of time elapsed between the time of the study and the mother's vitamin use was much shorter in the NICHD study therefore making it more likely that the women were able to recall accurately their vitamin history.

Another area of focus among studies of congenital anomalies is the infants of diabetic mothers. Central nervous system defects and malformations of the heart are much more common among babies born to diabetic mothers. The rate of these defects has risen significantly in recent years and is the leading cause of death in infants of diabetic mothers. Studies supported by NICHD indicate that diabetes-induced embryopathies are caused by one or more factors that disrupt normal intrauterine growth and development.

In another NICHD study, children born as a result of in vitro fertilization (IVF) were found to be at no greater risk of congenital malformation or developmental delays than other children. Researchers examined 83 children born as a result of IVF and 93 non-IVF children comparable in age, sex, race, maternal age, and whether they were a single birth, twin or triplet. All the IVF children were conceived at the Eastern Virginia Medical School in Norfolk between October 1983 and September 1985, while the non-IVF participants were randomly selected from babies born within a 100-mile radius of Norfolk.

The children were examined for both physical and mental development between 12 and 30 months of age. Malformations found in two IVF children and one non-IVF child were not considered statistically significant. Dr. James Mills, NICHD epidemiologist and one of the authors of the report, concluded that the study offers assurance to parents that IVF children should function as well as other children of similar social and economic background.

National Cancer Institute

In 1989, the National Cancer Institute recently funded a study (currently in its fourth year of implementation) designed to reduce smoking among pregnant women, a primary prevention technique for reducing low birth weight and infant mortality.

Numerous studies have established maternal smoking as a principal cause of low birth weight, and in turn, low birth weight as a primary cause of infant mortality.

Dr. Richard Windsor at the University of Alabama Comprehensive Cancer Center in Birmingham, Alabama, and colleagues are studying the effects of active, smoking cessation techniques among low-income women in four clinics operated by the Jefferson County Health Department in the Birmingham, Alabama area.

Preliminary study findings are very promising. In the initial sample of 400 women, cessation rates of 16 percent were achieved in the intervention group, compared with a 4 percent rate in women who did not receive special help with smoking cessation.

A cost-benefit analysis revealed considerable potential health care cost savings, even if just 12 percent of the approximately 350,000 pregnant smokers who annually receive publicly supported health care were to stop smoking. Based on estimates from the Office of Technology Assessment and considering only the babies of the 12 percent of quitters, the total excess publicly supported health care utilization cost of caring for these low-birth-weight babies during the first year of infancy would be over $17 million. Alternatively, intervention costs for materials and staff to be used with the U.S. public health birth cohort of pregnant smokers would be $1.7 million, resulting in a cost-benefit ratio of 1 to 10.

National Heart, Lung, and Blood Institute

The National Heart, Lung, and Blood Institute (NHLBI) supports research on infant mortality in the area of neonatal respiratory distress syndrome, a breathing disorder that causes disability and death in premature infants.

Synthetic Lung Surfactant Authorized for Treatment of Neonatal Respiratory Distress Syndrome

A synthetic surfactant was developed by investigators supported by an NHLBI Specialized Center of Research grant to Dr. William Tooley at the University of California, San Francisco, and manufactured by the Burroughs Wellcome Company under the name "Exosurf." Clinical trials of exosurf were begun in 1984, and recent results have shown that treatment of premature infants with the synthetic surfactant is associated with significant improvements in lung function and a reduction in mortality from neonatal RDS. Although Exosurf has not been approved formally by the Food and Drug Administration (FDA), it has been released by the FDA under a new program to speed potentially life-saving treatment to patients critically ill with conditions for which no satisfactory standard therapy exist. Successful treatment with Exosurf results in reduced periods of mechanical ventilation for infants with RDS, thereby decreasing the chances of complications from that procedure. Future work will involve testing the efficacy of synthetic surfactant in the treatment of other respiratory conditions of newborns, including pneumonia and acute lung injury.

Surfactant Differences May Explain Differences in Prenatal Lung Maturation and Incidence of Neonatal RDS in Blacks and Whites

Black infants are known to have lower rates of RDS than white infants, despite the higher incidence of premature and low-birth-weight infants among blacks. Investigators supported by an NHLBI Specialized Center of Research grant to Dr. Mary Ellen Avery, Brigham and Women's Hospital, Boston, Massachusetts, are working with scientist from Nigeria to explore the possibility that there is a difference in lung surfactant between the races and that this difference might help to explain the lower rates of RDS in blacks.

Initial studies using probes for genes that code for the proteins associated with lung surfactant have revealed racial differences in the genetic patterns for one of the surfactant proteins. The finding is preliminary and needs to be confirmed in further studies. If confirmed, however, it may help to explain the earlier maturation of the lungs of black infants and the rarity of RDS among premature black infants weighing more than 1,500 grams. Moreover, if accurate and reliable genetic markers of lung maturation can be determined, they should enhance the ability to predict which individuals, either black or white, at risk of delayed lung maturation.

National Institute of Neurological Disorders and Stroke

Brain hemorrhage affects nearly one half of low-birth-weight infants and is a significant cause of mortality and morbidity in newborns. The National Institute of Neurological Disorders and Stroke (NINDS), is the focal point for research on the causes and prevention of this serious disorder.

Dr. Henrietta Bada, an NINDS grantee at the University of Tennessee in Memphis, has investigated the use of the drug indomethacin to prevent brain hemorrhage in infants. During a controlled trial with 120 low-birth-weight infants, Dr. Bada found that babies treated with indomethacin experienced less severe hemorrhaging and had reduced levels of circulating prostacyclin, a compound found in the blood that contributes to increased blood flow and helps prevent blood clots.

Because these findings point to indomethacin as a potential preventive of brain hemorrhage, NINDS is funding further evaluation of this promising drug. Grantee Dr. Laura Ment of Yale University in New Haven, Connecticut, is conducting a multi-center, controlled trial of indomethacin in low-birth-weight infants. Her study will assess long-term health benefits of the drug, as well as its efficacy in preventing and limiting cerebral hemorrhage.

National Institute of Allergy and Infectious Diseases

Each year, 5 to 10 million of the world's infants and children die of gastrointestinal diseases, largely the result of bacterial and viral infection. Singling out the organisms that cause these infections and identifying methods to prevent them is a mission of researchers whose work is conducted and supported by the National Institute of Allergy and Infectious Diseases (NIAID).

Mother's Milk as a Weapon Against Bacterial Disease

Diarrhea caused by bacterial infection takes the greatest toll among gastrointestinal-related deaths in infants. Although researchers have already established a positive association between breast feeding and reduced incidence of diarrheal disease, how human milk inhibits microbial activity is still unclear. Furthermore, scientists have yet to define the full spectrum of diarrhea-causing microbes susceptible to the effects of breast milk.

NIAID researcher Dr. Stephen A. Dolan and his co-workers at the University of Missouri-Columbia in Columbia, Missouri, undertook a study to determine which bacteria respond to milk's inhibitory effect and whether different strains of these bacteria react similarly. The researchers obtained milk from seven nursing mothers who had given birth 1 week to 3 months previously. Multiple strains of four diarrhea-causing types of bacteria were then cultured with either the milk whey, commercial infant formula, or soy broth. For most of the strains tested, milk whey proved to be far more potent than formula in reducing bacterial multiplication. On the other hand, in assays of the bacteria *Campylobacter jejuni*, the researchers found that formula was the stronger inhibitor.

Dr. Dolan's work shows the value of exploring methods to increase the protective effects of breast milk, either by immunizing the mother or providing her with nutritional supplements. The immunization approach is supported by animal studies, particularly a recent study that demonstrated the feasibility of protecting a newborn calf from cholera by immunizing its mother. In addition, Dr. Dolan's work study highlighted the potential of improved infant-feeding formulas. For example, in communities with a high prevalence of bacteria not susceptible to the protective effects of breast milk, supplemental feeding with formula developed for enhanced inhibitory capabilities could be of immense benefit to newborns.

Virus Related to Animal Pathogens May Cause Illness In Human Babies

To devise a strategy for preventing life-threatening disease, scientists must first find the microbe responsible for infection. In cases of diarrhea caused by a virus, the process for identifying the culprit can be extremely difficult for a number of reasons: the viral particles themselves tend to be too small or of insufficient quantity to be detectable; many types of virus do not grow in tissue culture; and the immune system responds differently to each type of pathogen, making it difficult to predict at what point in the infection process the body will secrete the viral particles scientists need for study.

Dr. Robert Yolken at the Johns Hopkins University School of Medicine in Baltimore, Maryland, specializes in diagnosing viral diseases. His most recent findings, in research contracted by NIAID, involve members of the viral genus *Pestivirus*, known to cause intestinal disease in animals, but never documented as a cause of illness in man. In animal studies, these microbes have been known to cross bovine placenta and infect the fetal calf.

Rather than attempting to detect the virus itself, Dr. Yolken devised an assay to detect the viral antigen, a substance in the invading virus that triggers the body's immune system to produce antibodies, which protect against the virus. When an antibody recognizes a particular antigen, the body's immune mechanisms stimulate a chemical reaction, serving as an indicator that a viral antigen is indeed present.

The Indian Health Service Hospital at Whiteriver, Arizona, provided Dr. Yolken's study population, which consisted of 128 babies under 2 years of age with diarrhea. Previous researchers found that half of the diarrhea cases in this group could not be attributed to a known organism. Under a study protocol that involved a complex series of assays, which included running control samples consisting of antibodies against several other diarrhea-causing viruses, Dr. Yolken found that of the 128 babies in the study, samples from 30 tested positive for bovine *Pestivirus* antigen.

Most of the babies who tested positive were less than a year old, and compared to the rest of the group, more required hospitalization. Dr. Yolken found that a large portion of the group also had respiratory complications, a factor that not only serves as a possible diagnostic indicator, it suggests that an infection previously unknown in humans could have severe consequences for human infants.

National Institute of Environmental Health Sciences

There is ample scientific evidence demonstrating that children during prenatal and postnatal development are particularly sensitive to environmental agents. During the pre- and postnatal period the child is dependent on the nutrients provided by the mother, either through the placenta prior to birth or through breastfeeding after birth. Thus, the National Institute of Environmental Health Sciences (NIEHS) is concerned about the effects of environmental agents on the mother and child during development, as well as the changes that occur in the metabolism of environmental agents during pregnancy. The NIEHS is particularly concerned about the mechanisms through which an environmental agent causes toxicity.

The N-nitroso compounds (NNO) are a class of ubiquitous environmental pollutants. These compounds are present in things like side-stream cigarette smoke, bacon, food preservatives, cosmetics and shampoos. Thus, there are few, if any, humans unexposed to these pollutants. Animal models have demonstrated that NNO compounds are developmental toxicants causing injuries to the central nervous and musculoskeletal systems. Dr. Elaine Faustman, an NIEHS grantee at the University of Washington in Seattle, is developing an in vitro model to study the mechanism of toxic effects of these compounds on developing systems.

Polynuclear aromatic hydrocarbons (PAHs) are another class of major contaminants found in industrial and urban environments. Specific PAHs are found in most smokes. Thus, human exposure to PAHs from various sources and activities is extensive. It is known from animal studies and epidemiological studies of women who smoke cigarettes during pregnancy that PAHs are toxic and may be teratogenic agents. The mechanisms for these and other effects are not well understood. NIGHS grantee Dr. Mrinal Sanyal at Yale University in New Haven, Connecticut, has initiated a study to determine how PAHs may be teratogenic. Initial studies suggest that smoking alters key enzymes that metabolize environmental chemicals to products capable of placental or fetal toxicity. These studies are important because previous hypotheses suggested that these enzymes were involved in chemical detoxification and thereby protective of the fetus.

Another potential hazard to the developing fetus revolves around modern agricultural practices, which include intensive use of pesticides and other types of agricultural chemicals for enhancing crop yield. Many of the pesticides used are thought to have teratogenic/mutagenic potential. Human exposure to agricultural chemicals can occur through ground water and pesticide residues on food, as well as through air-borne exposure at the time of application. Dr. James Beaumont, an NIEHS grantee at the University of California, Davis, is conducting an epidemiological study in the San Joaquin Valley in California to assess possible relationships between fetal death and pesticide

exposure during pregnancy. One specific endpoint being followed in this study is the potential correlation between low birth weight and pesticide exposure.

NIEHS scientist Dr. Allen Wilcox is using data from a prospective study of early pregnancy to explore factors that affect fertility. In a series of studies, Dr. Wilcox and his co-investigators have found that women exposed prenatally to their mother's cigarette smoking are substantially less fertile as adults. Methods for detecting early pregnancy developed by NICHD grantee Dr. Robert Canfield at Columbia University in New York and used in the NIEHS study, may provide a sensitive means for detecting reproductive effects of some environmental hazards. Dr. Wilcox and his colleagues also observed for the first time that women who consume greater amounts of caffeinated beverages take longer to get pregnant. He is now collaborating in a study correlating the time it takes to get pregnant and with caffeine consumption among women in an _in vitro_ fertilization program.

Other studies are planned to examine in detail the reproductive performance of women who were exposed _in utero_ to diethylstilbestrol (DES). These women have been identified as having a high frequency of abnormalities of the reproductive tract. The study cohort is from the largest controlled clinical trial of DES use for pregnancy support; thus, it comes with a natural comparison group, and should allow more valid conclusions than have been possible previously.

National Institute of Arthritis and Musculoskeletal and Skin Disease

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) research focuses on several potentially fatal diseases that affect the bones, joints, muscles, or connective tissues or infants. The advances described here include research on the inherited blistering skin disease called epidermolysis bullosa, or EB, and on osteogenesis imperfecta (OI), a disorder of connective tissue in which affected infants are abnormally susceptible to bone fractures.

In research on EB, Dr. D. Martin Carter at the Rockefeller University in New York, in collaboration with the Food and Drug Administration, led a multi-center trial to test the efficacy of the drug phenytoin (an anticonvulsant) for the treatment of recessive dystrophic EB. This form of EB is quite severe; many times almost all body surfaces are covered by blisters and may be virtually devoid of normal skin. Scarring of the mucous membranes in the esophagus interferes with passage of food into the stomach, causing anemia, malnutrition, and retarded growth. Because past research had suggested that a phenytoin decreases an enzyme that is abnormally produced in EB, it was hypothesized that this drug might be effective for patients with the disease.

Overall, the trial failed to show a therapeutic benefit from phenytoin in patients with EB. The researchers found no difference in the size or number of blisters when the patients received phenytoin or when they were on a placebo. Phenytoin was effective only in reducing the number of tissue erosions seen in the patients. Because of the toxic side effects of this drug, the researchers could not recommend the use of phenytoin unless a patient on the drug showed a marked improvement. Other candidate drugs for EB now are being evaluated in animal models to find a more effective treatment for this disease.

In other EB research, the NIAMS-supported National EB Registry was used to search for gene defects in patients with recessive dystrophic EB. Dr. Jo-David Fine at the University of Alabama in Birmingham, who directs one of the centers of the registry, used genetic technology to show an association between patients with this type of EB and their tendency to inherit a particular gene cluster more often than do persons without the disease. The researchers are continuing to use the registry to study additional patients to determine the precise gene mechanism(s) underlying this disease.

NIAMS-supported research Dr. Jeffrey Bonadio at the University of Michigan, Ann Arbor, has applied new techniques to analyze gene mutations in infants born with perinatal lethal OI or OI type II. These newborns have very fragile connective tissue because of faulty production of collagen, a protein which contributes to bone strength and organization. These babies are

extremely fragile and experience multiple bone fractures even in utero. Dr. Bonadio found that the defective collagen in perinatal lethal OI results from an amino acid substitution in the gene, which alters the way the protein is assembled. The techniques of polymerase chain reaction (PCR) that were first applied to studying collagen genes in this investigation can be used to study the other types of OI and will allow more rapid determination of the structure and function of the complex collagen molecule.

Division of Research Resources

The Division of Research Resources (DRR) supports a wide range of research aimed at understanding the causes of infant mortality. A major effort at General Clinical Research Centers (GCRC's) is focused on examining the complications of premature birth.

GCRC's provide the research infrastructure for multidisciplinary studies on both children and adults. Specifically, they provide patient research facilities, computerized data management and analysis, as well as research nurses, dietitians, biostatisticians, and specialized laboratories for the translation of basic and clinical research into medical practice.

It has been established that infants born prematurely often develop bleeding in the brain. The clotting and inflammation that result can clog the passages that allow fluids to drain naturally out of the brain's ventricles. This can lead to hydrocephalus, commonly called water on the brain. As fluid accumulates, brain tissue is squeezed, and, unless the pressure can be relieved, damage may result.

A new test that exactly measures the volume of fluid in brain ventricles has been developed by DRR grantee Dr. Benjamin Brann and his associates at the University of New Mexico GCRC in Albuquerque. Ultrasound images of ventricles are traced into a computer. Computer software written by Dr. Brann and his colleagues calculates the ventricle size and computes the volume of fluid. This volume is compared to others calculated from previous images, allowing fluid accumulation to be easily detected.

According to Dr. Brann, more than 70 infants have been successfully monitored with this new technique. More than 20 showed signs of hydrocephalus. Without the computer tracking technique, ultrasound images must be visually compared by the physician, who then must estimate whether the ventricles are getting bigger.

Dr. Brann notes that an exact record of fluid accumulation showing trends is important because about half of all cases of hydrocephalus regress without damaging brain tissue. Surgery to drain ventricles is particularly dangerous when done on premature infants. Therefore, physicians need to identify the newborns at risk of being injured by the accumulation of fluid. Careful monitoring of these patients with ultrasound and computer analysis of the images can provide an exact record of fluid in infants who have experienced brain bleeding, Dr. Brann concludes.

Another concern with premature babies is that they are often deficient in surfactant, a substance necessary for lung expansion and tissue elasticity. DRR grantee Dr. T. Allen Merritt and his

associates have been administering natural human surfactant to very premature infants at risk for developing respiratory distress syndrome (RDS), which is caused by this deficiency. According to Dr. Merritt, this treatment lessens the severity of pulmonary illness, which often follows RDS, and prevents more RDS-associated deaths than does conventional ventilatory therapy alone.

In collaborative studies at the University of California GCRC in San Diego, the University of Helsinki and the Hospital of the Midwifery Institute in Helsinki, Finland, human surfactant was sprayed into the lungs of about 30 very premature infants who were at risk of developing severe RDS. The treatment significantly decreased morbidity and mortality among these infants compared to a similar group that did not receive the treatment.

Premature infants are also susceptible to streptococcal infections, particularly those caused by group B beta-hemolytic streptococci (GBS). These bacteria cause early onset disease, characterized by progressive respiratory failure, pulmonary hypertension, and cardiovascular collapse. Recently the toxic components of a poison generated by these bacteria were identified, clearing the way for the development of methods to treat or prevent this disease, which is fatal in a third of affected premature infants.

NATIONAL CENTER FOR NURSING RESEARCH

The National Center for Nursing Research (NCNR) supports research and research training on methods to reduce infant mortality by developing better nursing techniques to help maintain or improve health during pregnancy, prevent preterm birth and low birthweight, provide optimum care for preterm and low birthweight infants, and promote infant health.

Dr. David L. Olds, of the University of Rochester Medical Center in Rochester, New York, is studying the effects of prenatal and postpartum nurse home visits on the health and well-being of poor pregnant women living in an urban area and their first-born children. The NCNR grantee and his research team are seeking to determine whether nurse home visits can help prevent many problems that contribute to infant mortality, such as prematurity and low birthweight, growth and nutritional problems, accidents, acute infectious illnesses, and child abuse and neglect.

The investigators will compare two groups of about 700 black women during pregnancy. Both groups will receive transportation for prenatal care, but one group will also receive regular prenatal visits from a nurse. These visits will be aimed at reducing cigarette smoking, drinking, and non-prescription drug use during pregnancy, and fostering healthy weight gain. The investigators hope to achieve a higher rate of treatment for infections or hypertensive disorders, increased preventive care and fewer emergency-room visits, more support from family members and friends and less depression and anxiety in the mothers in the home visitation group.

For two years after delivery, one group of 250 women will receive regular postnatal visits from a nurse as well as sensory and developmental screening for the children. The investigators will assess the effects of the nurse visits on the mothers' child care practices, as well as on their mental-health functioning, their use of health and human services, the number of unintended pregnancies, and their reliance on welfare. These women will be compared to a group of 500 women who after delivery receive only screening services for their children.

The researchers will look at whether prenatal and postpartum nurse home visits will reduce government expenditures by helping to avoid the high costs often associated with maternal and child dysfunction.

This study replicates a previous one by Dr. Olds, done in a rural area, which involved nurse home visits to young white pregnant single women and their first-born children. That study showed that nurse home visits in this type of population can help prevent many problems which would place infants at higher risk of mortality.

Outlook

While it is disappointing that the nation did not reach the 1990 goal set for infant mortality at the beginning of the decade, significant progress was made toward that achievement. The U.S. had an all-time low mortality rate in 1988, and remarkable progress was made over the past 10 years in our ability to save the lives of premature and sick newborns.

Research directed specifically at reducing infant mortality has intensified in recent years. This research has led to advances in medicine and patient care as well as yielding powerful new technological tools with which to combat the problem.

Applying these advances and employing the new technological tools ensures that much progress will be made in the coming decade, with the hope that the goals set for infant mortality for the year 2000 can be realized.

CENTERS FOR DISEASE CONTROL

Infant Mortality

The infant mortality problem in the U.S. is reflected by the slowing decline in the rate of infant mortality, the continued disparity in infant mortality rates between blacks and whites, and the lack of progress in reducing the incidence of low birthweight (LBW). Low birthweight is not only the primary contributor to infant mortality but also results in significant economic costs to society. Approximately 6% of all live births are of low birthweight. These births account for neonatal intensive care costing $1.7 billion annually. The average cost per admission for a low birthweight infant is approximately $15,000. These costs are but a fraction of the total economic costs resulting from this condition when permanent development and physical impairments are considered.

Low birthweight is associated with maternal health behaviors during pregnancy, such as the use of cigarettes, alcohol misuse, and poor nutritional practices. For instance, over 900,000 children are born each year to women who smoke, a practice that doubles the risk of low birthweight and increases the risk of stillbirth or neonatal death by up to 100%. It is estimated that 10 percent of infant mortality is attributable to maternal smoking. Cessation of these health risk behaviors has been shown to have a positive effect on birth outcome by reducing the incidence of low birthweight.

CDC conducts surveillance and epidemiologic investigations, and provides program development and technical assistance, to reduce perinatal, neonatal, and postneonatal mortality and morbidity related to low birthweight, sudden infant death syndrome (SIDS), prematurity, congenital defects, and complications of pregnancy. In partnership with States, efforts are directed at reducing adverse pregnancy outcomes by identifying risk factors and developing and evaluating interventions to target these factors. Analytic support is provided to link birth/death certificates with key Maternal and Child Health (MCH) Program data to permit monitoring of program coverage, targeting, and effectiveness.

Smoking Cessation in Pregnancy (SCIP)

Since 1986, CDC has worked closely with the Colorado, Maryland, and Missouri State health departments to develop and implement programs to assist pregnant women attending public health clinics to quit smoking. Major accomplishments to date include:

- Demonstration projects are underway throughout each State. Preliminary data from the first 1537 patients in Colorado indicate that the quit rate at the 8th month of pregnancy is 13.7% in intervention clinics and 9.2% in control clinics. Among prior smokers who quit before enrollment, 90% of intervention and control patients are still not smoking at the 8th month.

- State-of-the-art interventions have been developed that require no additional staff to implement, and include patient counseling at every visit, self-help materials, and individual guidance identifying support for stopping smoking.

- States are committed to continuing the smoking cessation after the demonstration phase and to expanding the program to include the clinics now serving as controls.

CDC has also in the past undertaken two Secretarial initiatives to protect the fetus and the child from the effects of cigarette exposure. In consort with four medical societies, 6.5 million English-speaking pamphlets, a million pamphlets in Spanish, more than 500,000 posters, and 400,000 donated stickers have been distributed to physicians, hospitals, and WIC and other clinics. Support for these initiatives has included national public service advertising on TV, radio, and in medical journals. These materials are still available and currently being distributed to the public.

CDC Infant Health Initiative

To help States better address the infant health issues outlined above, a comprehensive surveillance system will be initiated to (1) identify those populations at highest risk, (2) enable States to target their intervention efforts, and (3) provide a data resource for evaluating progress towards the Year 2000 Objectives related to low birthweight and infant mortality.

Two substantial enhancements are underway for existing surveillance work, to better address these infant health issues.

- The Pregnancy Nutrition Surveillance System (PNSS) is an ongoing program-based surveillance system designed to monitor the prevalence of nutrition-related problems and behavioral risk factors among high risk prenatal populations. This effort, initiated in 1979, is designed to improve the management of State prenatal programs. Program managers use PNSS information to target high-risk, prenatal subpopulations for interventions and to evaluate the effectiveness of interventions designed to reduce specific factors related to low birthweight. Programs participating in the PNSS include the Special Supplemental Food Program for Women, Infants, and Children (WIC) and prenatal clinics operated under the Maternal and Child Health Block grant. Presently, data related to height, weight, weight gain, and hematocrit/hemoglobin, as well as smoking and alcohol behaviors are being collected in 26 States plus the District of Columbia, Puerto Rico, and American Samoa.

- The Pregnancy Risk Assessment Monitoring System (PRAMS) has been instituted in six States. PRAMS is an ongoing, population-based surveillance program of mothers who have recently delivered a live-born infant. Using birth certificates, States select a sample of mothers who are contacted by mail or telephone within 4-5 months after delivery. Mothers are asked about their prepregnant and prenatal behaviors, their experience of complications during pregnancy, and their use of health care during pregnancy and the first months of the infant's life. Data collection has begun in six States. A workshop held in March 1989 evaluated the first phase data collection methods and operating procedures.

These efforts will significantly increase State capacity to monitor health-related behaviors associated with poor pregnancy outcome, to use the information to direct intervention efforts more precisely and efficiently to

those areas and populations in greatest need, and to enhance State capacity for maximizing the use of readily available clinic information for programmatic purposes.

State Capacity Building for MCH Surveillance

Because programs to reduce infant mortality are implemented at the State level, an essential CDC function is to improve the States' capacity to direct surveillance, investigations, program evaluation, and prevention efforts, as well as improve service delivery. CDC provides technical assistance for States to target and effectively serve high-risk groups. Over the past 4 years, CDC has provided long-term support to four of the States with the highest infant mortality rates (Mississippi, Alabama, South Carolina, Georgia) through the assignment of epidemiologists to work with maternal and child health directors and has provided short-term assistance to New York City, New Jersey, Kentucky, West Virginia, Arkansas, Iowa, Hawaii, Montana, Utah, Puerto Rico, and the District of Columbia.

Severe Malnutrition

Malnutrition and its effect on childhood morbidity, growth, and development is another important public health issue. There are few data available on the extent, etiologies, and risk factors associated with a problem that is made even more complicated by lack of a satisfactory definition of hunger or malnutrition in the domestic setting. Most of the data currently available are based on small case studies from which prevalence estimates cannot be made, nor can the determination of risk factors and etiologies.

In 1973, CDC developed a system for the surveillance of nutrition problems among low-income children coordinated through State health departments. Since then, the Pediatric Nutrition Surveillance System has grown from an initial 5 States to the present 42 State participants. This system uses data from children who participate in the Women, Infants, and Children Supplemental Food Program (WIC) and in other Maternal Child Health Programs which are targeted toward low-income families. These data have provided extensive information to enable States to identify nutrition problems among children who participate in these programs. On the other hand, many children who are eligible do not attend, and there is concern that if some of the most needy are not reached, there may be cases of severe malnutrition that are missed by existing data collection methods. Specifically, there is presently no mechanism in place for identifying cases of severe pediatric malnutrition that are seen and treated in hospitals or other acute care facilities.

CDC is working with four States (Florida, Louisiana, Massachusetts, and Mississippi) to assess the feasibility of a system to detect cases of severe malnutrition in hospitals and, potentially, in other health and social service care facilities as well. The long-range goal of these collaborative efforts will be to determine the feasibility or mechanisms that can be implemented more broadly in other States and localities to establish ongoing surveillance of severe malnutrition among low income, high-risk children.

Goals and objectives of the Surveillance of Severe Pediatric Undernutrition (SSPUN) program include identifying surveillance catchment areas, determining population-based SSPUN prevalence rates and risk factors, documenting the process of creating such a system, and developing a feasibility model of SSPUN for application to other States. Active case definition from multiple reporting sources (e.g., hospitals, WIC clinics, child abuse reporting systems, emergency shelters) has been initiated to identify cases of severe pediatric under nutrition in the catchment area.

INFECTIOUS DISEASES/HEPATITIS B
INFANT MORTALITY

Hepatitis B has a disproportionately high incidence among blacks, Hispanics, Pacific Islanders, Alaskan Natives, Asian-Americans and Asian immigrants. Defining the risk of HBV infection in various minority groups has been approached in several ways. The Sentinel County Study of Viral Hepatitis and the Viral Hepatitis Surveillance Program (VHSP) provide information on the incidence of infection and risk factors associated with infection among ethnic groups. The prevalence of HBV infection has been defined from serologic studies of the National Health and Nutrition Examination Survey (NHANES II), Hispanic HANES and in other special epidemiologic studies of Asian populations.

A vaccine demonstration project and a statewide Alaskan Native vaccination program initiated in 1981 and 1983, respectively, have markedly reduced the annual incidence of disease among Alaskan Natives. Persons vaccinated in 1981 are being followed annually to identify new infections and measure antibody levels, and thus determine the need (if any) for a booster dose of hepatitis B vaccine. Immunogenicity studies utilizing various vaccines, dosage amounts, and schedules are planned. Hepatitis B surface antigen carriers are being followed and tested annually with alpha-fetoprotein (AFP) to detect early, resectable liver cancers. A vaccine demonstration project in American Samoa (1985) established the screening of pregnant women for HBsAg and the treatment of their infants, provided HB vaccine for all susceptible persons in the population, and integrated HB vaccination into the routine childhood immunization program. In other Pacific Islands affiliated with the U.S. (Guam, Saipan, Palau, Micronesia), hepatitis B immunization programs have been initiated (1988) through the cooperative efforts of the local public health departments, the Department of Interior, local Maternal and Child Health Programs, and the US Public Health Service (Region IX and CDC).

In 1988, the Immunization Practices Advisory Committee (ACIP) recommended that all pregnant women in the U.S. be screened for HBsAg to prevent mother-to-infant transmission of HBV. Of the estimated 18,000 pregnant women who are found to be HBsAg positive each year, 48% are Asian, 19% are black and 11% are Hispanic. Beginning in FY 1990, resources will be available to states to supplement programs designed to screen pregnant women for HBsAg, provide HB vaccine and HGIG to their infants, and screen and vaccinate susceptible household contacts.

Also occurring in particularly high incidence among Alaskan Natives are meningitis, pneumonia, septicemia, and other diseases due to invasive H. influenzae and S. pneumoniae. A statewide laboratory-based surveillance of all isolates of these organisms from sterile sites (blood, spinal fluid, etc.) is ongoing. Data from surveillance include confirmation, serotyping and antibiotic sensitivity testing. A program is currently underway in cooperation with one Native regional health corporation to assure vaccination of all persons at high risk for pneumococcal disease and enhance blood culturing practices in the region. To reduce H. influenzae disease in Alaskan Native children, BPIG (bacterial polysacharide immune globulin) is being administered to all infants in one service unit. In another area, the four available H. flu-conjugate vaccines are being evaluated in immunogenicity trials.

In addition, invasive cervical cancer is diagnosed in Alaskan Native women at more than twice the rate of that of the U.S. white population. Studies are underway to determine the overall prevalence of infection of human papilloma virus (HPV) infection and the specific types of infection in women with cancer, those referred to colposcopy clinics, and women undergoing routine Pap smear. A case control project is also ongoing to determine risk factors for cervical neoplasia.

Other infectious diseases of particular significance to minority populations include plague, dengue, sickle cell anemia, and Human Parvovirus B19 infections. Plague is an acute bacterial infection spread to humans by wild rodents and their fleas. The disease occurs most commonly in Hispanic and native American populations in Arizona and New Mexico. The major efforts to contain this disease include active surveillance and development of educational programs targeted to Hispanic populations and native American tribes in the southwestern United States. Epidemic dengue and dengue hemorrhagic fever, transmitted by the Aedes Aegypti mosquito, are a major disease problem in Puerto Rico and throughout the Caribbean Basin. Ongoing programs for prevention and control of dengue include surveillance, mosquito containment initiatives, and widespread community education programs. Sickle cell anemia and human parvovirus B19 infections occur predominantly in blacks and Orientals. CDC involvement includes outbreak investigation and epidemiologic studies.

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National Center for Health Statistics

NATIONAL MATERNAL & INFANT HEALTH SURVEY

The National Maternal and Infant Health Survey (NMIHS) is designed to obtain in-dept information on maternal risk factors (smoking, prenatal care, etc.) and their relationship to infant mortality and low birth weight. Starting with a recorded pregnancy outcome (live birth, fetal death, or infant death), NCHS contacts mothers, physicians, hospitals, and other scurces of care to obtain information. Sources provided the health habits of the mother, medical history, drugs and medications used during pregnancy, obstetrical procedures, complications, and access to prenatal care. This survey, that began data collection in 1988, is being conducted by NCHS under collaborative funding arrangements with 15 other sponsoring agencies.

CENTERS FOR DISEASE CONTROL

National Center for Health Statistics

LINKED BIRTH AND INFANT DEATH RECORD PROJECT

The Linked Birth and Infant Death Record Project is a project of the National Center for Health Statistics (NCHS) carried out is cooperation with State vital statistics offices and the Association of Vital Records and Health Statistics.

The NCHS Linked Birth and Infant Death Record project will produce and evaluate microlevel national linked data for four birth cohorts, 1983-86. A related project called the National Infant Mortality Surveillance (NIMS) project was conducted by the Division of Reproductive Health, Center for Chronic Disease Prevention and Health Promotion, CDC. This project developed interim national linked data for the 1980 birth cohort. Prior to these projects, such data have not been available nationally since a special study was conducted by NCHS using data from the birth cohort of 1960.

The linked record data system supplements information from death certificated of infants with information from their birth certificates. This includes characteristics of the infant at birth such as birth weight and gestational age, and characteristics of the mother such as her age, educational attainment, and marital status. The system enables NCHS and the States to provide important information on infant deaths, not available from death certificates, but recommended by the World Health Organization (WHO). The system will provide an important national data base to study the correlates of perinatal and premature infant death; and it will provide needed information to measure progress toward the 1990 and Year 2000 National Objectives for maternal and infant health.

Information from these linked files allows us to understand better what is achievable in reducing infant mortality by comparing infant mortality rates among subgroups of mothers. For example, we can divide the white and black populations into three risk groups:

- Low- married women aged 20 and over with 13+ years education and early prenatal care.
- High - unmarried teenagers and high parity mothers with less than 12 years education.
- Moderate - all others.

The infant mortality rate increases steadily with increasing maternal risk in both the black and white populations. Furthermore, postneonatal mortality comprises a larger portion of all deaths with increasing maternal risk. If all women were able to achieve the infant mortality rate

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experienced by the lowest risk group in each race, there would be 30% fewer infant deaths among blacks and whites. Much of this reduction could be accomplished by reducing postneonatal mortality among infants of normal birth weight, an objective which should be achievable with increased access to primary pediatric care.

The 1985 birth cohort national linked file is being evaluated for quality and completeness. It will be available by March 1990. The 1986 birth cohort national linked file will be available by the end of FY 1990.

Infant Mortality (HIV)

CDC is addressing the problem of pediatric AIDS in several ways. Surveillance for pediatric HIV disease is being conducted through: 1) expanded efforts in national surveillance of HIV infection and AIDS in infants and children, including surveillance for all HIV infection in selected cities and States to better define the extent of the problem in this population; and 2) HIV seroprevalence surveys in neonates in 45 States and in young children attending outpatient clinics in the cities of New York, Washington, and Miami. Ongoing studies in New York and Newark of children born to HIV-infected mothers are seeking to define risk factors for transmission of HIV from mother to child, evaluate new tests for diagnosis of HIV in infants, and better describe the course of the disease in infants. These children will also enter into treatment trials whenever possible. A study of women of childbearing age in a south Florida community with a high HIV prevalence will evaluate their sexual practices and possible approaches for supporting behavior change that will reduce the risk of infection in these women and their children.

In addition, Perinatal AIDS Prevention Projects have been funded to encourage the effective use of contraception among those HIV-infected women and women at high risk of infection who wish to avoid pregnancy. Eight Perinatal AIDS Prevention Projects, totaling over $4,800,000, were funded in fiscal year 1989 and will continue to be supported in fiscal year 1990. These projects will: 1) determine and seek to overcome obstacles to effective use of contraception among target populations; 2) facilitate the use of family planning services among the target population; 3) evaluate attitudinal factors related to use of contraception among HIV-infected and high-risk women; 4) encourage behavioral change among HIV-infected and high-risk women to reduce risk of acquisition or transmission of HIV.

In FY 1991, the eight Perinatal AIDS Prevention Projects will be funded at $7,899,000. In addition, an initiative to prevent HIV Transmission among women will be funded at $14,000,000.

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LONG-TERM CARE

Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
Public Health Service:					
Health Resources and Services Administration:					
Bureau of Health Professions.....	$288,658	$159,608	$575,367	$444,199	---
Alcohol, Drug Abuse, and Mental Health Administration	17,969,000	23,148,000	4,417,000	4,909,000	4,080,000
Agency for Health Care Policy & Research					
Nat. Ctr. for Health Services Research.	4,944,001	3,983,826	1,758,000	5,980,000	6,670,000
TOTAL, PHS.....	23,201,659	29,291,434	6,750,367	11,333,199	10,750,000
Health Care Financing Administration 2/	10,548,000,000	11,622,000,000	12,688,000,000	14,541,000,000	16,036,000,000
Office of Human Development Services.	200,000	1,600,000	2,900,000 1/	2,900,000 1/	2,900,000
TOTAL.....	10,571,401,659	11,650,891,434	12,697,650,367	14,555,233,199	16,049,650,000

1/ Level of funding is dependent on second and third year continuation cost.
2/ Level is for institutional Long Term Care.

HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Health Professions

Long Term Care Activities

In FY 1989 the Area Health Education Center program awarded a total of $150,672 to eight projects with specific educational activities in long term care. An estimated 60,145 individuals will benefit as a result of this training.

One General Internal Medicine/General Pediatrics Residency grantee indicated specific training in long term care in which eight residents will participate.

Two Physician Assistant Training programs have activities targeted to exposing an estimated 26 students to the issues of long term care. No specific funds were identified for such program activities.

Seventy faculty will be exposed to long term care as part of the curriculum at 23 of the projects being supported under the new Geriatric Medicine and Dentistry Faculty Training program.

Long term care is part of the training offered by at least one of the AIDS Regional Education and Training Centers Program grantees.

Nursing Special Project grants funded three projects in the amount of $424,745 in FY 1989 to support a comprehensive geriatric nursing assistant training program; to increase the ability of nurses and nursing personnel in rural long-term care facilities to provide care to elderly residents with psychiatric problems and to provide training for nurses in infection control in nursing homes.

ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION

National Institute of Mental Health

LONG-TERM CARE

In the mental health field, long-term issues relate primarily to people with a severe and persistent mental or emotional disorder that seriously impairs their ability to function in their primary social and vocational roles--the population known as chronically mentally ill. It has been estimated that approximately three million persons age 18 and older suffer from severe and persistent mental disorders. Of these, 80 percent are moderately to severely disturbed, and 57 percent suffer prolonged, severe disability. It is estimated that between 1.0 and 1.1 million severely mentally disabled persons reside in private households.

Many of the older chronically mentally ill live in nursing homes. There are approximately 1.4 million nursing home residents, of whom approximately 1.1 million have Alzheimer's disease, related dementias, or other mental disorders. This number reflects a dramatic shift in the locus of care for the mentally ill elderly from State and county facilities to nursing and personal care homes.

LONG-TERM CARE PROGRAM ACTIVITIES

Extramural Research Activities

NIMH supports a broad range of extramural research on services for persons with mental illnesses that require long-term care. Centers for Research on the Organization, Financing, and Delivery of Care for the Severely Mentally Ill have been funded at Johns Hopkins University-University of Maryland, Rutgers University, University of Wisconsin, Oregon Health Sciences University, and the Western Consortium for Public Health in Berkeley. NIMH is also supporting a national evaluation of the nine-city Robert Wood Johnson Foundation Program for the Chronically Mentally Ill. The effectiveness of innovative programs generated by this demonstration and by the same Foundation's Mental Health Services Development Program, which is also focused on severely mentally ill persons, are being assessed.

Financing of long-term care is a major focus of the NIMH services research centers and of several research project grants. Investigators in Oregon, Minnesota, and New York are investigating the effects of using capitation as a means of reimbursing long-term care while Medicaid financing of services for the severely mentally ill is the subject of studies that are utilizing Michigan and New Hampshire data. Effects of social security income maintenance on lives of severely mentally ill persons are being studied by an investigator in North Carolina.

Other NIMH research is concerned with the effectiveness of services provided to severely mentally ill persons. Studies in South Carolina and California are assessing the cost-effectiveness of different types of community-based treatment programs for severely mentally ill persons, while a study in North Carolina involves development and testing of a model treatment program for autistic adults that is intended for eventual state-wide utilization.

A new center for research and knowledge dissemination on self-help mental health services has been established at the University of Michigan and other NIMH-supported research on self-help services is underway at the Western Psychiatric Institute in Pittsburgh. Additionally, help-seeking and services utilization by severely mentally ill persons are being examined by an investigator at Indiana University.

Research on services for persons with mental disorders that co-occur with alcohol and/or drug abuse disorders was the subject of a new research announcement issued in FY 1989 by NIMH, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Institute on Drug Abuse (NIDA). Five research grants and a research scientist award were funded for work in this area. Studies underway at the University of Massachusetts Medical Center, Beth Israel Medical Center in New York City, and Mercy Catholic Medical Center in Philadelphia are seeking to determine the most effective clinical mixes of alcohol, drug abuse, and mental health services for patients with multiple diagnoses. Cost-effectiveness of such services is being examined by investigators located at the Dartmouth University Medical Center and at the Santa Clara County Department of Mental Health and the Berkeley and San Francisco campuses of the University of California. A study at the University of North Carolina is investigating services use, treatment response, and compliance with treatment among adolescents with co-occurring psychiatric and substance abuse disorders.

Another new research announcement in FY 1989 invited State and territorial mental health authorities to submit applications for grants that could improve their capacities to conduct rigorous evaluations of their service programs for severely mentally ill persons. Eight grants were awarded to State agencies in California, Connecticut, Hawaii, Ohio, and Oklahoma.

Finally, a major contract was awarded to the Research Institute of the National Association of State Mental Health Program Directors (NASMHPD) to expand a multi-state project focused on collection of longitudinal data on state mental hospital patients. The contract will provide comparable and edited data tapes for the period FY 1988-1989 on patients in 15 states. This will be the first time so large a body of longitudinal data has been collected on a cohort of severely mentally ill persons.

Community Support Program (CSP)

Initiated in 1978, the mission of the NIMH Community Support Program (CSP) has been to work with States and localities to improve opportunities and services for adults with long-term, disabling mental illness. CSP focuses on adults who are inappropriately institutionalized in hospitals or nursing homes and the larger number of chronically mentally ill individuals who are living outside of institutions without adequate housing or life support services--estimated at 1.7 million to 2.4 million persons.

The program awards grants to State mental health agencies to focus on the needs of this population and to implement the administrative, budgetary, and programmatic changes necessary to improve community support and rehabilitation services. At present, all States, the District of Columbia, and two territories have had or are currently receiving funding for CSP efforts.

Beginning in 1986, in accordance with the new legislative authority of Section 504 of the Public Health Service Act, the program began to emphasize community services demonstration projects. In FY 1986 and FY 1987, three-year projects were funded to focus on local service approaches for elderly mentally ill persons, homeless mentally ill individuals, mental health consumers, and young adults with mental illness and substance abuse problems. In addition, 21 States that had completed CSP strategy development were awarded small service system improvement grants in order to continue CSP-related activities on behalf of the long-term mentally ill. In FY 1988, projects focusing on housing, self-help, and comprehensive system approaches were funded. In FY 1989, the program placed greater emphasis on the research component of service demonstration projects. Nine projects with rigorous research designs were funded to test various approaches to providing case management services, one to test community crisis response services, and one to test psychosocial rehabilitation services. In addition, nine States were awarded new CSP Service System Improvement grants.

Other activities undertaken in FY 1989 included:

- Joint funding (NIMH and the Department of Education's National Institute on Disability and Rehabilitation Research) of a new 5-year funding period for the rehabilitation research and training center at Boston University. The center will undertake new projects in the areas of case management, self-help, and vocational rehabilitation;

- Implementing a national evaluation of the five CSP-supported Housing Demonstration Projects through a grant to the University of Vermont;

- Issuing and disseminating new publications on the topics of residential services, consumer self-help and involvement,

client outcome research and cost-benefit analysis for community support services;

- Supporting initiatives to promote involvement of mental health consumers in the service system, such as a national teleconferencing project, a technical assistance project and clearinghouse, a national conference on self-help and consumer involvement;

- Working with State staff and national consumer leaders to develop a model principles and mission statement for commissioners of mental health to use in promoting self-help and consumer involvement in their respective states;

The NIMH Protection and Advocacy Program

Public Law 99-319, the Protection and Advocacy For Mentally Ill Individuals Act of 1986 (re-authorized and amended by P.L. 100-509, 1988), authorizes NIMH formula grant allotments to Protection and Advocacy (P&A) systems which are designated by the Governor in each state to protect and advocate the rights of mentally ill individuals in residential facilities and to investigate incidents of abuse and neglect.

P&A systems are independent of any agency providing mental health treatment or services; of the 56 P&A Systems, 45 are private, not-for-profit organizations, and the remainder are State agencies which operate outside of the State service delivery systems.

In fiscal year 1988, P&A systems served a total of 15,042 individual clients. The majority of clients (81 percent) were between 21-64 years old. A little more than two-thirds of all clients were living in public mental hospitals at the time they contacted the P&A agency.

Allegations of Abuse were present in 23 percent (N = 5,303) of the complaints investigated. The most frequent complaints concerned inappropriate or excessive medication and physical assault. Three hundred sixty three deaths were reported and investigated. The vast majority (N=276) of these cases were handled by the New York State P&A system which is vested by the State with responsibility to investigate all instances of deaths occurring in residential mental health facilities.

Allegations of Neglect were included in 45 percent (N = 10,340) of the total number of complaints handled. The most frequent charges were failure to provide appropriate admission to a residential facility, failure to provide appropriate medical/mental health treatment, and failure to provide discharge planning.

Rights protection issues were present in 38 percent (N = 7,657) of the total complaints handled. The most frequent complaints

concerned finances and reimbursements, legal representation and housing.

A total of 18,407 information and referral services were provided by P&A agencies, and an estimated 96,559 people benefitted from public education and/or constituency training activities including training on patients' rights for staff of residential facilities, presentations on P&A and patients' rights to residents of mental health facilities, ex-patient/consumer groups, and family members, and public education outreach to address issues such as discrimination and stigma.

P&A systems in 25 States were involved in class action litigation to benefit an estimated 278,361 clients. Forty-five systems reported involvement in legislative advocacy (e.g., reviewing, commenting and testifying on proposed State legislation), most frequently concerning involuntary commitment procedures. Fifty-four systems were active in systemic advocacy (e.g., negotiations to revise Departmental and hospital policies), particularly on obtaining least restrictive therapeutic settings, protecting patient rights in proposed transfers, and ensuring P&A access to client records.

Priority areas for fiscal years 1989-90 include increasing outreach and services to Blacks and Hispanics and developing new strategies to respond to advocacy needs for children.

State Human Resource Development and Planning

The State Human Resource Development (SHRD) Clinical Training Program awards grants to State departments of mental health to use cost-effective and realistic approaches to improve the availability, distribution, competence, and appropriate utilization of personnel who provide mental health services to severely and chronically mentally ill adults, seriously emotionally disturbed children and youth, mentally ill offenders, the elderly and/or minorities. The program promotes linkages between mental health and related service agencies; institutions that educate, train, or otherwise prepare mental health personnel for the delivery of mental health services; and organizations responsible for licensure, certification, and reimbursement policies and processes affecting the deployment and utilization of the mental health services' work force.

The State Comprehensive Mental Health Services Planning Program assisted States in the development of comprehensive plans to better meet the needs of adults and children with severe mental illness. These plans require the development of an organized community-based system of care, the establishment of targets regarding the implementation of such a system, a reduction in the rate of hospitalization of the seriously mentally ill, and a mechanism for evaluating the State's progress toward these goals.

In November 1986, President Reagan signed P.L. 99-660, establishing the new State mental health planning mechanism and authorizing grants to the States to develop comprehensive State mental health service plans for the severely mentally ill. States are required to submit to the Secretary annual State plans for establishing and implementing organized community-based systems of care for the severely mentally ill for fiscal years 1988 through 1991. Submission of the plans occurred on January 10, 1989. The plans were reviewed and the second round of plan submissions is currently underway.

As also required by the law, a model plan for a community-based system of care for mental health consumers has been produced. An informal advisory group provided advice and consultation to the Institute on this task. This group included State Mental Health Directors, providers of mental health services, severely mentally ill individuals, advocates for such individuals, and State mental health planners. The model plan framework is now complete and is presently being disseminated to the States.

For many of the severely mentally ill, the service delivery system appears to be too fragmented to provide accessible, coordinated, long-term care. Furthermore, because the financial burden for these conditions is often substantial, research efforts are needed to identify reimbursement mechanisms to support coordinated services. NIMH is nearing completion of a new research initiative to improve care of the severely mentally ill. The plan is expected to stimulate expanded efforts in clinical services research, service systems research, and a variety of activities to find ways to make the care of severely mentally ill individuals more effective. The planning process, begun in the spring of 1989, has drawn in expert advisers from all parts of the country to consider and recommend ways in which mental health services research can contribute to meeting the needs of this population. Their report will be completed in 1990.

AGENCY FOR HEALTH CARE POLICY AND RESEARCH

Formerly the
National Center for Health Services Research
and Health Care Technology Assessment

LONG TERM CARE

The Agency for Health Care Policy and Research (AHCPR) was established on December 19, 1989 as a separate Public Health Service (PHS) agency by the Omnibus Budget Reconciliation Act of 1989, P.L. 101-239. As authorized under a new Title IX of the PHS Act, the purpose of the agency is to enhance the quality, appropriateness, and effectiveness of health care services and to improve access to such services. This will be accomplished through the establishment of a broad base of scientific research and through the promotion of improvements in clinical practice and in the organization, financing, and delivery of health care services. The new agency replaces the former National Center for Health Services Research and Health Care Technology Assessment.

As the leader of Federal efforts in outcomes research and health services research, the AHCPR seeks to create and disseminate new knowledge and better understanding of the processes by which health services are made available and how they may be provided more efficiently and effectively. The AHCPR conducts and supports scientific research that tests the assumptions on which current health policies and practices are based, assesses the performance of the health care system, and examines alternate ways to organize, finance, and deliver health services. AHCPR's program is directed towards the needs of health care policymakers, providers, and consumers. It addresses the full array of health care issues, among them long term care.

With the aging of the population, the technical advances in medical care, increased survival among both the young and the old, and the prospect of a widespread epidemic of AIDS, the availability, costs, and financing of long term care services are major issues in public policy. The problem in this area will increase as more diagnostic and therapeutic innovations prolong life. The country now spends in excess of $40.0 billion for patients with Alzheimer's disease and related dementias. The costs for caring for patients with dementia associated with AIDS may dwarf these expenditures. Yet, despite the current and anticipated growth in expenditures for long term care, relatively small sums have been available to study how these services might be delivered more effectively and efficiently.

The goal of the AHCPR health services research program in long term care and health services for the aging is to develop alternative strategies for providing long term care that will reduce Federal expenditures for these services, increase their availability, and improve their quality. In FY 1990-FY 1991, AHCPR will undertake a number of initiatives to expand research

on long term care. Studies of home health care and the role of caregivers will be included in both the AHCPR intramural and extramural programs. AHCPR also will support studies that address a variety of questions on the economics of health care and the elderly.

Intramural Research

The aging of the U.S. population has heightened public and private focus on the health, social, and residential services required by individuals who have lost the ability to function independently because of ill health and physical and mental impairments. The increasing risk with age of incurring such impairments, coupled with the rapid growth of the elderly, will ensure that caring for the impaired elderly will continue to be an important issue for public and private policies.

The AHCPR intramural research program directly undertakes health policy research and analysis in three major areas: national health care expenditures and utilization, hospital costs and utilization, and long-term care. Staff of the intramural research program have been involved in research on the problems of financing long term care for a number of years. In addition, staff are conducting research on health, social, and residential services for physically and mentally impaired elderly.

Long Term Care Studies Program

Using such large data sets as the National Long Term Care Surveys, The National Morality Followback Survey, and the National Nursing Home Survey, the NCHSR's Long Term Care Studies Program undertakes studies on problems such as long-term care expenditures; the feasibility of alternative financing and reimbursement strategies; and the types of care that might be required for particular levels of functional disability. The following list reflects the FY 1989 publications and conference presentations of the Long Term Care Studies Program:

Authors: Murtaugh, C., L. Cooney, R. DerSimonian, H. Smits, and R. Fetter
Title : Nursing Home Reimbursement and the Allocation of Rehabilitation Resources
Source : Health Services Research, 1988.

Authors: Jackson, M.E., M.L. Drugovich, M.D. Fretwell, W.D. Spector, J. Sternberg, and R.B. Rosenstein
Title : Prevalence and Correlates of Disruptive Behavior in the Nursing Home
Source : Journal of Aging and Health, 1989.

Authors: Spector, W.D. and M.L. Drugovich
Title : Reforming Nursing Home Quality Regulation: Impact on Cited Deficiencies and Nursing Home Outcomes
Source : Medical Care, 1989.

Authors: Spector, W.D., M.C. Kapp, R.T. Tucker, and J. Sternberg
Title : Factors Associated with Presence of Decubitus Ulcers at Admission to Nursing Homes
Source : The Gerontologist, 1989.

Authors: Stone, R.
Title : The Feminization of Poverty and the Elderly
Source : Women's Studies Quarterly.

Authors: Kemper, P.
Title : Case Management Agency Systems of Administering Long Term Care
Source : Gerontological Society of America annual meeting

Authors: Murtaugh, C.
Title : Estimates of the Risk of Nursing Home Use in Later Life
Source : The American Public Health Association annual meeting

Authors: Sternberg, J. and W.D. Spector
Title : The Prevalence of Decubitus Ulcers: Issues of Concern
Source : National Pressure Ulcer Advising Panel Consumers Conference

Authors: Kapp, M.C. and W.D. Spector
Title : Risk of Rehabilitation and Subsequent Death for Elderly Nursing Home Residents
Source : Gerontological Society of America annual meeting

Authors: Spector, W.D., R.B. Rosenstein, W. Freiberger, and M. Kapp
Title : Functional Change and Discharge Status Patterns: New Admission Nursing Home Cohort
Source : Gerontological Society of American annual meeting

Authors: Spector, W.D. and C. Phillips
Title : Staff Turnover as an Indicator of Quality of Care in American and Australian Long-Term Care Facilities
Source : Gerontological Society of America annual meeting

Authors: Kapp, M.C., A.M. Eichorn, and W.D. Spector
Title : Quality of Care in Nursing Homes: Indicators for New York and Texas
Source : American Public Health Association annual meeting

Authors: Murtaugh, C. and R. Stone
Title : The Elderly Population with Chronic Functional Limitations: Implications for Home Care Eligibility
Source : American Public Health Association annual meeting

Authors: Stone, R. and P. Kemper
Title : Spouses and Children of Disabled Elders: Potential and Active Caregivers
Source : Gerontological Society of America annual meeting

Authors: Stone, R.
Title : Spouses and Children of Disabled Elders: Current and Future Patterns of Caregiving
Source : Conference on Caregiving in the 21st Century sponsored by Stanford University and the Veterans Administration conference

Authors: Stone, R.
Title : The Competing Demands of Caregiving and Employment
Source : American Society on Aging

Authors: Stone, R.
Title : Estimating the Size of the Disabled Elderly Population: Implications for Public and Private Long Term Care Insurance
Source : Conference on Long Term Care Insurance sponsored by Health Insurance Association of America, the American Association of Homes for the Aged, and the American Health Care Association

Authors: Stone, R.
Title : National Data on Informal Caregivers: Implications for State Long Term Care Planning
Source : National Association of Health Data Organizations annual meeting

Authors: Stone, R.
Title : Elder Care and Work: Legislative Initiatives
Source : Eastern Region of the Council of State Governments annual conference

Authors: Stone, R.
Title : Informal Caregivers of the Elderly: Barriers to Family Care
Source : Conference on Barriers to Family Caregiving sponsored by Duke University and the Alzheimer's Association

National Medical Expenditure Survey

In FY 1989, NCHSR continued work on the 1987 National Medical Expenditure Survey (NMES). This survey will provide a unique data base on how the population uses health care, what they pay for this care, and how we finance these expenditures. A substantial amount of new information on the elderly and long term care is being collected. The national household survey of the civilian noninstitutionalized population includes an oversampling of groups of particular policy interest, including the elderly. In addition to the core data on use, expenditures, health insurance, and sociodemographic variables collected for the noninstitutionalized population, the 1987 NMES household survey has a new focus on long term care. For example, data are being obtained on charges and sources of payment for both formal and informal caregivers and on various measures of health status and functional limitations of the noninstitutionalized long term care population.

The NMES provides a unique opportunity to examine the utilization and expenditures for long term care provided in the community and in institutions. To permit estimates of the utilization and expenditures associated with community based care, the Household Survey Component (HHS) of NMES was designed to include an oversample of elderly and functionally impaired individuals. Approximately 6,000 elderly and 13,000 functionally impaired elderly are included in the data. A parallel survey was conducted among 10,000 residents of nursing homes and homes for the mentally retarded. In both surveys, respondents were followed as they entered and were discharged from institutions.

Data from the Household Component

The NMES HHS questionnaire is designed to collect information concerning all utilization, expenditures, sources of payment for health care and insurance coverage in 1987. In addition to questions concerning use of physician-based services, visits to emergency rooms, outpatient departments, hospitalizations, and expenditures related to prescribed medicines and other medical expenses, data are collected on the use of and charges for home health services, including care provided by a medical person, a friend, relative, homemaker or home health aid.

Basic demographic information is collected for all respondents (e.g., race, gender, education). Of special importance for elderly health financing issues are questions of assets. Detailed income information (paralleling CPS income questions) as well as home ownership questions were asked. Data concerning house modifications related to functional impairments and the relationship between onset of functional limitations and selling a home were included in the study.

Functional ability and use of community-based care is measured at two points in time, during the first and fourth round of interviewing. The questions include the Activities of Daily Living and Instrumental Activities of Daily Living developed by Katz. Both measures of difficulty and the need for personal assistance of the use of special equipment are included in the instrument. Utilization of community-based care, such as senior centers, adult day care centers, enrollment in programs such as "meals on wheels," and use of special transportation designed for the elderly or handicapped are measured. Data are also available concerning supplemental income provided by friends or relatives not living in the household.

The data also include several questions concerning the effects of providing care to an elderly or functionally impaired person. These questions include the effects on employment (e.g., working fewer hours due to providing care, taking time off, the need to quit a job, the effect on income) as well as measures of stress related to such care (e.g., amount of free time, strain on income, effects on sleep). For those providing care to someone outside the household, additional items measure the types of care provided and amount of time spent delivering that care.

Condition information associated with disabilities and utilization are collected. In addition, measures of prevalence for several chronic conditions such as hypertension, arthritis, diabetes, emphysema, and heart disease are possible, regardless of whether the condition was related to utilization during 1987. Prevalence measures are also possible for developmental disabilities such as epilepsy, cerebral palsy, autism, and mental retardation.

Several of the data elements address the question of access to care. These questions include whether the person has ever or is currently on a waiting list for a nursing home and whether the person did not receive care for some reason when he or she needed it.

Institutional Population Component

Two institutional groups are included in the Institutional Population Component (IPC) of NMES: those individuals in nursing homes and those individuals in homes for the mentally retarded. The design of the IPC samples individuals at both the beginning of 1987 ("Current Residents") as well as throughout 1987 ("New Admissions"). This provides a sample base that includes both long-term residents as well as short-term residents and permits analyses concerning living arrangements and use of community-based care prior to institutionalization. Data have been collected on approximately 6,000 nursing home residents (3,350 current residents; 2,570 new admissions) and 4,500 residents of homes for the mentally retarded (360) current residents; 862 new admissions). Interviews were conducted both with an appropriate respondent from the institution and, whenever possible, with a

relative or guardian of the resident ("Next of Kin"). The next of kin reported on the health status of the resident prior to admission and use of community-based services.

The Baseline questionnaire, collected once per resident, obtains information on the resident's demographic characteristics, history of admissions to institutions and living arrangements prior to the present admission, current functional ability (the same ADL/IADL measures used in the HHS), the need for personal assistance or the use of special equipment related to the functional limitation, primary diagnosis upon admission, employment status prior to admission, and measures of prevalence for both developmental disabilities and chronic conditions similar to those asked of HHS respondents. All of the questions concerning health status (e.g., ADL measures) are recollected in the End of Year Questionnaire.

The Institutional Use and Expenditure Questionnaire is administered every four months. Information on all ambulatory care that residents receive both inside and outside the facility and for each general or short-term hospitalization are collected. Expenditure information, including source of payment and types of services included in the charge, is collected for charges associated with the institutionalization.

Detailed information concerning the resident's living arrangements, functional ability, use of special equipment, and income prior to institutionalization are provided by the next of kin. This questionnaire includes a set of questions with respect to providers of care in the home that parallel the HHS component (e.g., household residents who helped the resident with bathing or dressing).

The next of kin is also asked to report on the use of community-based services by the respondent. Utilization of health care services (e.g., physician's, emergency rooms, outpatient departments, etc.), prescribed medicines, and other medical equipment is collected as well as the associated total charges (per quarter) and the sources of payment.

The following bibliography reflects aging-related papers/publications completed by staff of the National Medical Expenditure Study in FY 1989:

Authors: Leon, Joel and Lair, Tamra
Title : The 1987 National Estimates of the Functionally Limited Elderly
Source : National Medical Expenditure Survey Research Findings 4

Authors: Lair, Tamra and Lefkowitz, Doris
Title : Characteristics of Nursing Home Residents: Findings from the 1987 NMES
Source : Annual Meeting of the Gerontology Society of America

Authors: Lair, Tamra et al.
Title : Mental Illness and Impact of Nursing Home Reform
Source : Annual Meeting of the Gerontology Society of America

Authors: Freiman, Marc et al.
Title : Nursing Home Reform and the Mentally Ill
Source : Annual Meeting of the American Public Health Association

Authors: Stone, Robyn and Short, Pamela Farley
Title : Effects of Care Giving for Disabled Elders
Source : Annual Meeting of the American Public Health Association

Authors: Leon, Joel and Short, Pamela Farley
Title : Use of Home and Community Services by Elderly Persons with Functional Disabilities
Source : National Medical Expenditure Survey Research Findings 5

Authors: Leon, Joel
Title : Availability of Special Nursing Home Programs for Alzheimer's Disease Patients
Source : Annual Meeting of the Gerontology Society of America

Extramural Research

The AHCPR extramural research program is carried out through peer-reviewed grants and contracts conducted at universities, at nonprofit organizations and institutions such as teaching hospitals, and by industry. In Fiscal Year 1989, a number of extramural research projects on issues related to developments in aging, the elderly and long term care were supported.

Projects Completed in FY 1989:

"Conference on Medicare and Research"
Mark Pauly, Ph.D., University of Pennsylvania, Grant No. HS05680

The Medicare conference held in October 1986 highlighted, through the delivery of invited papers and panel discussion, findings and issues dealing with Medicare and its effects on utilization, provider choice, and financing. The conference proceedings, entitled Lessons from the First Twenty Years of Medicare: Implications for Public and Private Sector Policy, was published in January 1989 by the University of Pennsylvania Press. Copies are

available from University of Pennsylvania Press at $34.95. Further information on the publication was included in NCHSR Research Activities, February 1989.

"Impact of DRGs on Public Home Health Nursing Services"
Elayne K. Phillips, Ph.D., University of Virginia, Grant No. HS05513

To study the impact of hospital prospective payment on the consumption of home health nursing resources. This study focused primarily on the changes in resource utilization in public home health since hospital implementation of the prospective payment system (PPS) by Diagnostic Related Groups (DRGs). Although the institution of DRGs was limited to Medicare recipients in hospital settings, preliminary reports suggested that changes in practice patterns were not limited to this population. Hospital patients were experiencing shorter lengths of hospital stay after prospective payment by DRGs and were discharged in less healthy states. Although providers had consistently reported shifts to more complex patients in home health patient populations, these changes had not been documented empirically. To begin this process, the current study investigated changes in requests for care and care delivered to public home health patients as related to the implementation of prospective payment by DRGs.

Two major research hypotheses were tested. First, that public home health nursing resource consumption would increase from the pre-DRG period to the post-DRG period. Second, that the increase in Medicare patients would be greater that non-Medicare patients. Twenty percent of all home health patients were randomly selected from health department home health patient referral logs across Virginia. This resulted in approximately 2,000 cases. Referral and billing forms were reviewed by registered nurses. Resource measures included frequency and number of nursing services requested, number and hours of billed visits delivered, and length of patient care episode. Analyses compared all groups pre- to post-DRG, and compared Medicare to non-Medicare groups. A subsample of approximately 300 Medicare cases was selected for additional study. Record reviews provided data on household composition, total nursing visits (billed and unbilled visits), and other nurse contacts, including telephone calls, conferences, and care related trips.

The following findings were reported: [1] The implementation of prospective payment by DRGs in hospitals was found to be associated with a significant increase in demand for home care. [2] Significant differences were found between Medicare and non-Medicare patients in the

utilization of home health resources and in outcome. [3] Variation in local area characteristics accounted for differences in resource consumption across agencies. [4] Analysis of the subsample revealed that on the average 1.5 unbilled nursing visits and 10 nursing contacts were made per episode, seven of which were telephone calls.

Conclusions are as follows: Public home health patients had more services requested after the implementation of hospital prospective payment by DRGs and these needs increased at a faster rate than did services delivered. Medicare home health patients did not appear to be selectively affected by the implementation of hospital prospective payment. In fact, the entire system was much more stable than anticipated.

Nevertheless, absolute differences in services requested and delivered are observed between Medicare and non-Medicare groups and between older non-Medicare and Medicare patients. Non-Medicare patients received more frequent, intense acute care, while Medicare patients received more intermittent, extended, chronic care. Among older patients, both Medicare and non-Medicare, needs for care were fairly uniform, reflecting a chronic, frail population. Older non-Medicare patients, who frequently had no ability to pay for care, received more aide visits and had more favorable outcomes.

The significant amount of heterogeneity existing across the state in requests for and delivery of care suggests that the community need for home health services cannot simply be determined by population size. Similarly, patient-level resource needs vary tremendously. Identification of high-risk communities and patients can be facilitated based on specific characteristics identified in this study.

The present amount of unbilled care delivered consumes a large amount of agency resources. The study suggests that unbilled care is an integral part of the structure and delivery of home health care. In the future, this care is likely to decrease due to agency pressure on staff to maximize reimbursable care. This component could be crucial to outcomes and deserves further study

The principal investigator developed recommendations for research, administration, education and policy development based on the findings and conclusions. This material will be reported on more fully in the literature.

"The Use of Medical Services and the Decision to Retire"
Charlotte Muller, Ph.D., Research Foundation, CUNY, Grant No. HS05729

To determine whether self-assessed poor health status is a rationalization or a reason for early retirement, this study compares health status of males reported before and after retirement in analyzing the relationship between the decision to retire and early death and between the decision to retire and the demand for medical care. The results show that the probability of dying within two years after retiring and the probability of seeking medical care at the time of retirement are much higher for retirees with health problems and especially for those retirees who report health problems and retire before 65. Work-limiting health problems, though self-reported are a reason for retirement. These findings are of importance given current policy to increase the retirement age. The results of this study are scheduled for publication in Health Services Research in the Spring of 1990. An AHCPR Research Activities Statement is in preparation for publication in 1990.

"Study of Chain Nursing Home Case-mix, and Staffing"
John Holahan, Ph.D., The Urban Institute, Grant No. HS05253

This grant originally looked at the effect of chain controlled nursing homes on cost, quality and access to long term care. However, the focus (but not the title) has changed to the effect of the Prospective Payment System (PPS) on access to nursing homes for Medicare patients, using data before and after implementation of PPS. The analysis is based on several separate but related analyses designed to examine different aspects of the access issue.

Although utilization of Skilled Nursing Facility (SNF) case increased between 1983 and 1985 as hospitals were being phased into the Medicare PPS system, Medicare covered SNF admissions declined. This finding indicates that increases in utilization of nursing home care by Medicare patients of SNFs were covered by other payers.

Results indicate that severity of the casemix of patients treated in Medicare SNFs increased over the 1983-85 period as hospitals were being phased into the Medicare PPS system. PPS appears to result in the discharge of a patient mix that requires greater SNF resources in PPS-covered states than in waiver states.

Medicare-covered SNF patients are considerably more costly to nursing homes than non-Medicare patients with the average cost of a Medicare-covered day in SNF-only facilities almost twice as high as a private inpatient day.

"Prospects for Caring for Persons with AIDS in Nursing Homes"
Rosalie Kane, University of Minnesota, Contract No. 282-87-0049

PWAs differ from a typical nursing home population in age, gender, stigmatized lifestyle, infectious nature of their disease, and need for complex medical care. To date, little systematic effort has been made to tap the perspective of those who live and work in nursing home, particularly the former.

In this study original data was collected from 100 nursing home residents, 100 nursing home responsible family members, and 100 nursing home direct care staff (N-300) in 16 Minnesota nursing homes, 8 of which were known to be willing to accept PWAs and a matched group that had not indicated such an intention. For the 3 samples, the investigators studied knowledge about and attitudes towards AIDS, and compared these to National Center for Health Statistics (NCHS) data about the general public. They also conducted detailed interviews with a small number of PWAs (N=4) about their nursing home experiences, and interviewed the administrators, directors of nursing, and directors of social work in the 16 homes (N=48) to further explore factors associated with the decision to treat PWAs in nursing homes and the experiences of facilities that did. These data were augmented by a literature review and a case study of expert opinion in the state and nationally.

Preliminary findings suggest that nursing home residents are somewhat less informed about AIDS than the general public, that nursing home residents' family members are similar in knowledge to the general public, and that nursing home staff (50 certified nursing assistants, 25 LVNs, and 25 RNs) are somewhat better informed than the general public. On the other hand, substantial misinformation and apprehension about AIDS exists in all three groups. With some exceptions, there were few differences in knowledge and attitudes in respondents associated with the 8 homes that were willing to serve PWAs compared to respondents associated with the comparison group facilities. In all categories, significantly more respondents in the homes that admitted PWAs stated they had met a PWA, but many of the residents and families in homes admitting PWA were unaware of the facility's policies.

Some, but not all line staff express fear of contagion, a fear also echoed by residents and family members. Some, but by no means all, residents expressed negative attitudes toward gays and drug abusers. In all categories interviewed, those who indicated they knew a PWA were mor positive and knowledgeable than those who did not. The PW interviewed expressed a wide range of negative reactions to the nursing homes environment, and respondents in all

categories suggested possible changes to make the nursing home more conducive to caring for PWAs. Considerable support was expressed for special nursing home units for PWAs.

Concerns of nursing home executive staff regarding care for PWAs were similar to those found in the literature reviewed. They included 1) inability to meet physical needs of PWAs, 2) inability to meet psychological and social needs of PWAs; (3) concerns about cost of care and inadequate 3rd party reimbursement; (4) concerns about a negative reaction from geriatric clientele; and (5) legal concerns.

Projects Ongoing in Fiscal Year 1989:

"Variations in Patterns of Primary Care Among the Elderly"
Charlyn D. Black, M.D., Johns Hopkins University, Grant No. HS06099

This dissertation research grant is a retrospective analysis of existing research data derived from 1) claims data from a provincial health insurance program, (the Manitoba Health Services Commission) and 2) survey responses that have been linked to claims data for elderly individuals (The Manitoba Longitudinal Study on Aging). Ambulatory claims will be used to operationalize four important attributes of primary care: first contact care, comprehensiveness, coordination, and longitudinality. The measures will be validated by examining relationships between the four measures, and be comparing scores for these attributes with survey responses that capture individuals' assessment about these aspects of their general medical care. Correlational and inferential analyses will be used in the analyses. The four attributes of primary care will be assessed by examining the degree to which age, sex, health status, educational, and monthly income explain variation.

Achievement of the objects may contribute to fostering more useful and credible research on the impact of primary care. The potential to quantify patterns of primary care allows linking information about variations in patterns of primary care with cost and effectiveness data, and to advance our understanding of the impact of primary care.

"The Use of Durable Power of Attorney in the Nursing Home"
Jiska Cohen-Mansfield, Ph.D., Hebrew Home of Greater Washington, Grant No. HS06090

This small grant examined the preferences of elderly nursing home residents regarding the health-care decision-making process. It investigated: (1) Preferences

for the choice of an agent for health-care, decision-making; (2) preferences for future life sustaining treatment; and (3) factors that might have influenced their preferences, such as previous experience with life sustaining treatments, religious beliefs, and personal values.

One hundred three residents of a large suburban Jewish nursing home participated in the study. Each participant was interviewed and several close-ended questionnaires were administered. In the interview, residents indicated the identity of their preferred decision-maker for health care and decided whether to formally execute a durable power of attorney. In the Preferences for Life-Sustaining Treatments Questionnaire, participants reported their preferences for or against four life sustaining treatments under three hypothetical levels of future cognitive functioning.

Results showed that participants tended to choose a son or daughter as their agent for future health-care decision-making. In most cases, this person was their closest relative. Subjects had clear and consistent patterns of preferences regarding the utilization of life-sustaining treatment. Generally, subjects would not opt for treatment. They were less inclined to opt for treatment as their future level of cognitive functioning declined, or when the anticipated treatment was applied on a permanent rather than a temporary basis.

"Practice Variation in Care of Arthritis"
Curtis Henke, Ph.D., Institute for Health Policy Studies,
Grant No. HS05912

This study will use existing data from an ongoing longitudinal survey to examine variation among rheumatologists in their use of medical and surgical hospitalizations as a part of the treatment of patients with rheumatoid arthritis. The specific aims are to: [1] measure variation in the observed hospitalization rates and the extent to which it is related to differences in the medical, functional, and socio-economic characteristics of rheumatoid arthritis patients and to the incentives of the physician's practice; [2] estimate parameters representing each rheumatologist's individual practice style in decisions to hospitalize; [3] measure the stability of practice styles and overall practice variation from year to year; [4] estimate the relationship of practice styles to training and practice characteristics; and, [5] determine whether differences in practice style are associated with differences in total treatment costs and patients' functional outcomes.

This study will have an impact on the clinical management of rheumatoid arthritis (RA). While it focuses only on hospitalization and surgery as outcome measures, the

findings could help in the design of a more comprehensive study of RA therapy. The results should provide important insight and could serve as a model for confirmatory studies in other settings.

"Case Control Study of Aged Users and Non-users of Home Health Care"

David Rabin, M.D., Georgetown University, Grant No. HS06049

This study will determine whether persons over age 60 who use home health care services differ significantly from non-users, in terms of functional status, spousal and social support, and sociodemographic characteristics. Data from the 1984 Supplement on Aging to the National Health Interview Survey will be analyzed using a case control methodology to compare those reporting use of home health care services (e.g. visiting nurses, home health aids), with those reporting use of other community services (e.g. meals on wheels) and no community services use.

Home health care is becoming an issue with major policy implications. While the majority of care has been provided in the past by informal caregivers (family and friends), with the increase in the aged population and concomitant aged potential caregivers, this will place a greater demand on the formal care providers (home health agencies). This study will provide insight on changes by informal care providers between the analysis of the 1982 Long Term Care Survey by NCHSR Intramural Researcher Robyn Stone ("Exploding the Myths: Caregiving in America") and the 1984 Health Interview Surveys. It will also provide a basis for interpreting the 1988 National Medical Expenditure Survey (NMES) Home Health Component that does not specifically address home visits by nurses.

"Effects of Advance Directives in Medical Care"

Lawrence Schneiderman, M.D., University of California at San Diego, Grant No. HS05617

The effects of an advance directive will be determined by a longitudinal, randomized experiment of 100 experimental and 100 control subjects all of whom have life-threatening illnesses. The experimental subjects are being offered the opportunity to execute an advance directive by their physicians; the controls do not receive an offer. All subjects are measured to determine levels of satisfaction, health status, health locus of control, utilization of health services and costs of care at intake, three months, six months, one year and tow years. Analyses will be carried out within the context of the General Health Policy model.

The study is expected to show that an advance directive will increase patient satisfaction and control, have no effect on patient's health status, and decrease cost by not using expensive life-sustaining forms of care that it is believed can have no demonstrable effect on patient health for a specific subset of terminally ill patients.

New Starts in Fiscal Year 1989:

"Impact of Toileting Dependence on Home Health Charges"
Dorothy J. Baker, Yale University, Grant No. HS06291

This dissertation research grant will retrospectively examine data already collected on a cohort of 8,000 low income elderly persons in the state of Connecticut receiving home care through a special program (Promotion of Independent Living) administered by the state's Department on Aging during the period 1982-1986. Four sources of data will be used: Medicaid and Medicare records, PIL records, nursing home admissions, and state data. Multivariate analyses will be used to examine how the following variable influence the use of services: patient activities of daily living (ADL), availability of informal social support, availability of long-term care services in the community, and use of inpatient hospital services.

This study is expected to make unique contributions to the currently rather sparse literature on determinants of use and costs of home care. The special emphasis on examining dependence in toileting is warranted by the special burdens it places on patients and on informal and formal caregivers. Despite growing recognition of the importance of this particular set of problems, previous research has only indirectly estimated its cost implications. Moreover, most evidence is based on the experience of populations residing in nursing homes. This unique data set and the results of the analyses will provide valuable insights that may influence home care policy and may help to motivate further clinical research addressing the problem of incontinence.

"Home Health and Nursing Home Market Analysis"
Charlene Harrington, University of California at San Francisco, Grant No. HS06174

Secondary data from Medicare and Medicaid and other sources and primary data to be collected on state policies and bed supply for the period 1986-1988 will ba used for this study. By building upon previous HCFA and NCHSR studies, the project will develop a ten-year cross-sectional time series data base of both secondary and primary data for 1978-88. A pooled cross-sectional time series regression

analyses will be conducted to examine differences within the ten-year time period. The analyses will use both integral and dynamic equation models of the home health and nursing home markets developed by the investigators to test a series of specific hypotheses regarding the nature of the two markets.

This study will produce papers designed for policymakers to consider in making changes in Medicare and Medicaid program policies. The descriptive analysis will provide valuable new primary data on state Medicaid nursing home and home health reimbursement rates and methods and total state nursing home bed supply not available from other sources. This study will examine the trends in state spending during the ten-year time period, and examine differences in pre- and post-Omnibus Budget Reconciliation Act of 1981 (OBRA) and pre- and post-DRG periods. The analyses will develop a better understanding of the market forces, which is said to be needed by researchers, industry officials, and policymakers.

"Urban/Rural Differences in Elderly Use of Long-Term Care"
Dr. Charles McConnel, University of Texas Southwestern Medical Center, Grant No. HS06197

Dr. McConnel will establish the extent and determinants of differences in survival and utilization of health and community based services by the rural/urban elderly. Data from the Longitudinal Study of Aging, the Census of the Population, the National Death Index, and the Health Professionals Resource File will be linked. A single analysis will then link a defined population data by health status, health services access, and health services utilization. The outcome variables include: physician visits, nursing home admissions, home health and/or nursing visits, homemaker services, use of community services and hospitalization.

"Functionally-Limited Elderly Living Alone: Access to Help"
Charlotte F. Muller, Ph.D., Research Foundation, CUNY, Grant No. HS06030

This study examines whether disabled elderly living alone differ in the availability of informal care, functional limitations and economic resources from elderly living with others. Additional research questions include not only the effect of caregiving on women's employment, but also the effect of employment on the amount of time given to informal care. Data sources include the 1982 and 1984 national Long Term Care Survey.

Preliminary findings indicate full-time employment substantially decreases the time allocated to informal care. Information from this study will aid in strengthening public policies aimed at maintaining the disabled in the community.

"Living Wills for Primary Care, AIDS, and Cancer Patients"
John D. Stoeckle, Massachusetts General Hospital, Grant No. HS06120

The objective is to assess whether comprehensive living wills are practical and desired by physicians and patients, and to provide some models for how they can handle the process of indicating preferences for care, and develop a model for living will format.

Three groups of patients will be surveyed about issues pertaining to living wills. The groups are: 388 patients seen in primary care physicians' practices; 291 patients with AIDS and 410 patients from a telephone registry. The first two groups will be interviewed by their physicians during regularly scheduled office visits, while the third group will be interviewed by telephone. The survey will be re-administered after six to 12 months, as well as after any interim hospitalization. In future follow-up on the cohorts used in the proposed study (not covered by the current funding), the investigators would seek to ascertain the impact of the living will on hospital costs of terminal care.

The specific goals of this proposal are: (1) to improve the format of available predrafted living wills by allowing individuals to specify preferences based on several hypothetical scenarios (2) to assess patients' interest in discussing terminal care issues, as well as their perceptions of barriers to such discussion; (3) to assess the extent to which patients have, and wish to have, living wills; (4) to assess how durable (reliable) patients; preferences are; and (5) to measure any changes inpatients' attitude regarding living wills as a consequence of participating in the survey (by self-report).

"Measurement of Preferences for Life-Sustaining Treatment"
Richard F. Uhlmann, University of Washington, Grant No. HS06343

The objective of this project is to measure the validity and reliability of patient preferences for life-sustaining treatment and states near to or worse than death, to identify the medical interventions, and health and social states which form the domain of content for advance directives, as well as the factors which influence their acceptability.

This study has three phases. In Phase I, 50 patients, 10 well adults, 15 physicians, and 15 nurses will receive a semistructured interview to identify the relevant content for advance directives and to pretest methods for Phase II. In Phase II, 250 patients and 100 well-adults will be administered a structured interview to scale their preferences for states and medical interventions, and evaluate the construct validity, predictive validity, and internal consistency of their preferences. In Phase III, patients and well-adults will be reinterviewed two weeks and six months following their enrollment in Phase II to evaluate the test-retest reliability and predictive validity, respectively, of their preferences. Patients will include persons with the acquired immunodeficiency syndrome, terminal illness, elderly with chronic disease, cognitively impaired, and nursing home residents. Physicians will be selected from a variety of primary care and subspecialty practices. Nurses will be selected from intensive care, inpatient, outpatient, home health, and nursing home practices.

Results will be directly applicable to the development of valid, efficacious, and effective advance care directives. In addition, they will provide an improved basis for understanding the validity and reliability of preferences contained in advance directives.

HEALTH CARE FINANCING ADMINISTRATION

Long Term Care

The mission of the Health Care Financing Administration (HCFA) is to promote the timely delivery of appropriate, quality health care to its beneficiaries--approximately 47 million aged, disabled, and poor Americans.

Medicaid and Medicare are the principal sources of funding for long term care in the United States. The primary types of care reimbursed by these programs of HCFA are skilled nursing facilities (SNFs), intermediate care facilities (ICFs), and home health services.

HCFA's Office of Research and Demonstrations (ORD) conducts research studies of a broad variety of issues relating to long term services and their users, providers, costs, and quality. ORD also conducts demonstration projects that demonstrate and evaluate optional reimbursement, coverage, eligibility, and management alternatives to the present Medicaid and Medicare programs.

RESEARCH ACTIVITIES

Long term care research activities in ORD can be classified according to five objectives:

- examining and promoting alternatives to institutional long term care;
- assessing and evaluating long term care programs in term of costs, effectiveness, and quality;
- examining the effect of the hospital prospective payment system (PPS) on long term care providers;
- examining alternative payment systems for long term care; and
- supporting data development and analyses.

Prior research in long term care has highlighted the fact that disabled individuals prefer to remain in the community as long as possible and that they are able to do this, in large part, due to the care provided by informal caregivers, usually family. For a number of years, ORD has been funding research that has been examining the amount and types of services provided by family members. This research is continuing and includes examination of contributions from both public programs and private individuals (e.g., family members) for the support of the disabled in the community. Information is being sought about the resources needed to support the informal caregiver network in its efforts to avoid unnecessary institutionalization of relatives.

Because of the interest in promoting noninstitutional care, and the recent increase in the utilization of these services, ORD's research is also examining the quality and effectiveness of the services in the home setting. These efforts include comparison of the quality, case mix, and cost of noninstitutional as compared to institutional services, as well as the examination of home care provided under different payment arrangements, e.g., fee-for-service versus capitation. As part of these efforts, groupings of patients are being developed that have similar expected outcomes. Such groupings are essential since home health care serves so many different types of patients, some of whom may fully recover and some who, even under the best of circumstances, are still expected to continue to decline.

A major responsibility of ORD is assessing the effects of various Medicare and Medicaid long term care programs and policies. Among the areas where results are available are the hospice, swing bed, and home and community-based waiver program.

Since the implementation of PPS for paying hospitals, ORD has been assessing the effects of this change on other parts of the health care system. Included in this research is the examination of the effects of PPS on long term care case mix, utilization, costs, and quality. Changes in the supply of long term care providers are also being studied. Major research projects are underway to analyze the appropriateness of post-hospital care and the course and outcomes of that care. In recent years, there has been increased emphasis on examining episodes of care rather than utilization of just one type of service. Medicare files, which link hospital with post-hospital care, continue to be analyzed to provide information on trends in the utilization of post-hospital care since the passage of the PPS legislation.

In 1989 ORD awarded a major contract to conduct research concerning the impact on Medicare beneficiaries and their family members of needing or providing long term care services, as well as the impact of the quality of long term care services on acute care use. Another contract was awarded to conduct studies concerning the quality of home care services for the elderly.

DEMONSTRATION ACTIVITIES

In 1989, HCFA implemented a major demonstration aimed at testing the effectiveness of community-based and in-home services for victims of Alzheimer's disease and other dementias. This project focuses on the coordination and management of an appropriate mix of health and social services directed at the individual needs of these patients and their families.

Demonstrations also are being implemented to assess the impact of innovative reimbursement strategies to promote cost containment and foster quality of care. Efforts are also underway to identify more effective long term care quality assurance techniques and to improve the statistics and baseline information upon which future assessment of needs, problem identification, and policy decisions will be based.

Information follows on specific HCFA research and demonstrations.

Medicare Hospice Benefit Program Evaluation

Period:	September 1984-June 1989
Funding:	$ 1,295,156
Awardee:	Abt Associates, Inc. 55 Wheeler Street Cambridge, Massachusetts 02138
Investigator:	David Kidder, Ph.D.

This contract addressed many of the questions raised by the Tax Equity and Fiscal Responsibility Act of 1982 (Public Law 97-248) and Deficit Reduction Act of 1984 (Public Law 98-369). The evaluation studies were to determine whether or not the reimbursement method and benefit structure of the hospice benefit are fair and equitable and promote the most efficient provision of hospice care. Also, recommendations for legislative changes were to be made as appropriate. HCFA administrative data, Part A and Part B claims, plus hospice cost report data were used as the basis of several types of analyses. The final report addressed how the Medicare hospice benefit has affected the US hospice industry; whether or not hospice care as reimbursed by Medicare is a cost effective alternative to more aggressive or less intensive non-hospice interventions; what factors explain differences in hospice and non-hospice expenditures; and projections of effects of certain changes in the hospice benefit.

An interim report, entitled "Medicare Hospice Benefit Program Evaluation," is available from HCFA as Publication Number 03248 (September 1987). The final report, entitled "Medicare Hospice Benefit Program Evaluation: Final Summary Report," (July 21, 1989) has been submitted to National Technical Information Service. In FY86 the hospice benefit payments of $20 million for about 10,500 Medicare beneficiaries who elected the benefit were less than 1 percent of the total Medicare Part A expenditures. Overall, the study found neither any significant increase in costs nor any significant savings to the Medicare program attributable to the Medicare hospice benefit during the 1984 - 1986 period. The only unambiguous finding regarding hospice cost savings is that of the freestanding hospices, compared to net additional costs generated in the provider-based hospices. Levels of overall savings were entirely

due to leverage from the freestanding and Home Health Agency (HHA) based hospice beneficiaries, for whom savings were estimated to be strongly positive. Hospital-based and SNF-based hospice beneficiaries incurred net costs. Analysis of FY85 combined Part A and B expenditures found, after adjustment, no difference between conventional care patient costs and those of hospice benefit patients. Analysis of the non-random, usable Medicare hospice cost reports submitted in 1985 and 1986 show that the certified hospices are larger than are non-certified hospices (random, stratified sample), have lower average daily costs than non-certified hospices and considerably lower costs per discharge than non-certified hospices. The certified hospices that submitted cost reports generally experienced positive net Medicare revenues over the period under study, with 86 percent having positive net revenues from Medicare. A few hospices did suffer losses. Certified hospices were generally able to earn positive net revenues while conforming to the reimbursement and inpatient day limits of the Medicare program. A simulation suggests that the sample of non-certified hospices also would have profited under the benefit, with three-fourths expected to have earned positive net revenues had they participated in the Medicare hospice benefit.

Medicaid Home and Community-Based Waiver Programs for Acquired Immunodeficiency Syndrome Patients

Period: August 1988-April 1989
Funding: $ 54,679
Awardee: The Rand Policy Research Center
1700 Main Street
Santa Monica, California 90406
Investigator: Peter Jacobson, Ph.D.

Description: The purpose of this project is to develop a background paper that identifies major research questions for an evaluation of the utilization and expenditure patterns of acquired immunodeficiency syndrome (AIDS) patients in State Medicaid home and community-based waiver programs. The study will identify appropriate data sources, review available literature on State waiver programs, and identify major research questions that should be addressed. The project will explore the reasons why States with large AIDS patient populations have not sought Medicaid home and community waivers.

The project team has reviewed current, Medicaid AIDS waivers in the States of California, Hawaii, New Mexico, New Jersey, Ohio, and South Carolina. Contacts have been made with other States considering using the waiver program. The final report is near completion.

Efficacy of Nursing Home Preadmission Screening

Period: June 1988-September 1990
Total Funding: $ 376,698
Awardee: Brown University
Division of Biology and Medicine
Providence, Rhode Island 02912
Investigator: Mary E. Jackson, Ph.D.

In recent years more than 30 States have adopted some form of nursing home preadmission screening as a method of identifying target populations for receipt of community-based services that would be at risk of institutionalization in the absence of the community services. The purpose of this project is to evaluate a nursing home preadmission screening methodology being used by the State of Connecticut, to identify those persons who would be institutionalized if community-based services (under the State's Medicaid home and community-based services waiver program) were not available. The project will analyze the extent to which the screen accurately predicts the need for a nursing home level of care or an equivalent level of community care. It is anticipated that this study will result in refinements to the Connecticut instrument, thereby assisting in the placement of long term care clients in the most cost-effective setting. The project also is including several other States' preadmission screening instruments in the analysis.

During the first year, the predictive validity of Connecticut's Preadmission Screen decision rules was preliminary assessed by applying them to three data sets of control group patients from the South Carolina Community Long Term Care Project, the Georgia Alternative Health Services Project, and the National Long Term Care Channeling Demonstration. During the second year of the study, screening and assessment data for a 6-month cohort of aplicants to Connecticut's Community-Based Services program will be reviewed. Subsequent analyses of these data will significantly impact the planned revision of Connecticut's screen.

Impact of Home Intravenous (I.V.) Drug Benefits on Beneficiary Utilization of Services

Period: August 1989-February 1991
Funding: $ 300,000
Awardee: University of North Carolina at Chapel Hill
School of Pharmacy
Chapel Hill, North Carolina 27599-7360
Investigator:

This study will construct a longitudinal 3-year data base on home I.V. drug usage in North Carolina and Florida. The project will identify home infusion therapy drugs to be studied and survey

North Carolina and Florida home I.V. drug providers to identify the current volume, composition and source of payment for home I.V. drug therapy. A stratified sample of providers will be selected and site-visited. Patient charts will be reviewed and abstracted for information on diagnosis, diagnosis related groups (DRG), patient outcomes, etc. This project is in the developmental stage.

Study of the Costs of Case Management

Period: August 1988-May 1989
Total Funding: $ 33,061
Awardee: University of Minnesota
1919 University Avenue
St. Paul, Minnesota 55104
Investigator: Rosalie Kane D.S.W.

The term "case management" often is used in reference to a variety of approaches and settings involving coordination of medical and/or supportive services. This study prepared a synthesis of information on long term care case management and its costs. The report reviews case management models and data collected by 51 case management programs. Four dimensions of case management were identified: the nature of services provided; goals of the case management program; the reimbursement mechanism; and specific operational constraints. Using these dimensions, five empirical models of case management were identified: fee-for-service; private insurance; capitated/consolidated; public-funded with purchase authority; and broker. Data on case-management costs and cost determinants are presented. A theoretical model relating program incentives and outcomes was developed and the limitation of the data for estimating this model is discussed.

Study of Inappropriate Use of Medications by Medicare Beneficiaries

Period: August 1988-April 1989
Total Funding: $ 23,279
Awardee: University of Minnesota
1919 University Avenue
St. Paul, Minnesota 55104
Investigator: Roger Feldman, Ph.D.

This study synthesized the existing literature on health problems associated with the inappropriate use of prescription medications by the noninstitutionalized elderly population. The study explored the extent of present knowledge regarding the prevalence of such a problem, which medications are most likely to be prescribed or used improperly, and possible interventions that might lead to a reduction in medical problems associated with

inappropriate medication use by the elderly. The final report of the study suggest that, although the literature does not certify the extent of inappropriate medication use by elderly Medicare beneficiaries, it does suggest that overuse of medications, adverse drug reactions, drug interactions, and non-compliance are common in the elderly. The report recommends a research agenda which includes developing improved criteria for judging the appropriateness of medication use and applying these criteria to a population-based sample of elderly Medicare beneficiaries.

Research Synthesis and Recommendations on the Quality of Selected Long-Term Care Services and on the Relationship between Long Term Care Services and Reduced Acute Care Expenditures

Period: October 1988-November 1989
Funding: $ 234,542
Awardee: University of Colorado
1355 South Colorado Boulevard, Suite 706
Denver, Colorado 80222
Investigator: Robert Schlenker, Ph.D.

This study conducted research in response to mandates in section 207 of the Medicare Catastrophic Coverage Act of 1988 relating to (1) the quality of long-term care services (in community-based and custodial settings), and (2) effects of the provision of long-term care services on reduction of expenditures for acute health care services. The project objectives included the development of recommendations for additional research in these areas.

Two reports were prepared entitled, "Future Research on the Quality of Long Term Care Services in Community-Based and Custodial Settings" and "State Survey of Community-Based Care Systems." An additional report, which identifies recommendations for further research on the relationship between long-term care services and acute care expenditures, was submitted late in 1989.

Study of Home Health Care Quality and Cost Under Capitated and Fee-For-Service Payment Systems

Period: June 1987-June 1992
Funding: $ 1,683,773
Awardee: Center for Health Policy Research
1355 South Colorado Boulevard
Denver, Colo. 80222
Investigator: Peter Shaughnessy, Ph.D.

This project will compare the quality and cost of home health care provided under capitated and non-capitated payment systems for two groups of Medicare beneficiaries: clients admitted to home health care following a hospitalization, and those who have

not been in a hospital for at least 30 days prior to the initiation of home care. Process and outcome quality measures are being developed and will be used with patient-level resource use measures to assess cost effectiveness of care in the two settings.

The project is currently recruiting HHAs for the data collection phase. Data gathering is scheduled to begin in mid-1990. Secondary data detailing Medicare utilization and costs are being analyzed.

Development of Outcome-Based Quality Measures for Home Health Services

Period:	September 1988-December 1992
Total Funding:	$ 1,965,389
Contractor:	Center for Health Policy Research 1355 S. Colorado Boulevard Denver, Colorado 80222
Investigator:	Peter Shaughnessy, Ph.D.

Most efforts to evaluate home health care quality have focused on the HHA organizational structure or the process of care delivery but have neglected patient outcome measures as quality indicators. The purpose of this contract is to develop and test outcome-based measures or indicators of quality for Medicare home health services. The measures developed should be reliable and valid for use in monitoring and comparing quality of home health care across agencies recognizing possible confounding factors such as case mix. The measures that are tested will be selected from a broad range of possible approaches including general health and functional status measures, indicators that are linked to specific diagnostic conditions and/or services, and measures that are more practical and less costly to administer. Criteria that will be used in the selection of measures to be tested include feasibility, reliability, validity, impact on quality access, and the cost/burden of data collection to the HCFA and HHAs.

During 1989, the contractor prepared syntheses of existing quality assurance approaches and of prior research into quality of home health care and a report describing the detailed project design. Data collection is scheduled to start in early 1990. During 1989, the Robert Wood Johnson Foundation awarded a grant to the Center for Health Policy Research that is intended to complement this contract study; the grant focuses on developing quality measures for adult non-Medicare home care services and populations and uses clinical panels to identify potential measures.

Develop and Demonstrate a Method for Classifying Home Health Patients to Predict Resource Requirements and to Measure Outcomes

Period: June 1987-June 1990
Total Funding: $ 968,332
Awardee: Georgetown University
Georgetown School of Nursing
3700 Reservoir Road, N.W.
Washington, D.C. 20007
Investigator: Virginia Saba, RN, Ed.D

The purpose of this cooperative agreement is to develop a method for classifying and assessing Medicare patients receiving care in certified HHAs that will predict resource requirements and measure outcomes of care. An abstract form was developed to collect information concerning relevant indicators of resource requirements and outcomes. This form will be used to collect data from the home health records of approximately 9,000 Medicare patients recently discharged by approximately 600 HHAs, stratified by size, ownership, and geographic location. The data are being analyzed, using multivariate and statistical techniques, to determine which variables are most predictive of resource requirements. The selected relevant variables will be incorporated into an assessment and case-mix classification tool that categorizes patients according to predicted resource requirements. Patient responses to home health care will also be evaluated to develop a quantitative outcome measurement tool. A data base of participating HHA and Medicare patient characteristics will also be produced. The collected data are being analyzed. A final report is expected by September 1990.

Home Care Quality Studies

Period: October 1989-March 1993
Total Funding: $ 2,642,445
Contractor: University of Minnesota
School of Public Health
Box 197, 420 Delaware Street, S.E.
Minneapolis, Minnesota 55455
Investigator: Robert Kane, M.D.

The purpose of this study is to carry out research in regard to: (1) The quality of long-term care services in community-based and custodial settings, and (2) The effectiveness of (and need for) State and Federal consumer protections which assure adequate access to and protect the rights of Medicare beneficiaries who are provided long-term care services (other than in a nursing facility). The project will focus on in-home care, examining those traditional home health services which are reimbursed by Medicare and Medicaid, as well as personal care and supportive

services which have more recently been covered by Federal and State sources of funding. Key project tasks will include: (1) development of a taxonomy clarifying the various objectives/goals ascribed to home and community-based care, from the various perspectives of consumers, payers, and care providers; (2) development and feasibility-testing of a survey design which would measure the extent of need for, and adequacy of, home care services for the elderly; (3) a study of variations in labor supply and related effect(s) on home care quality, as well as factors that contribute to these variations; and (4) recommendations to improve the quality of home and community-based services by identifying "best practices" and promising quality assurance approaches. The contract was awarded on September 29, 1989.

Urban/Rural Variation in Home Health Agency and Nursing Services

Period: September 1989-August 1990
Funding: $155,096
Awardee: Brandeis University Research Center
415 South Street
Waltham, Massachusetts 02254
Investigator: Christine Bishop, Ph.D.

Brandeis University and The Urban Institute will compare urban and rural home health services and nursing home services to determine variation between provider characteristics and service utilization patterns. The underlying cost structures of urban/rural HHAs will be studied as well. This study is national in scope and will utilize several Medicare data bases for analysis.

Analysis of Costs, Patient Characteristics, Access and Service Use in Urban/Rural HHAs

Period: September 1989-August 1990
Funding: $103,240
Awardee: University of Minnesota Research Center
420 Delaware Street, S.E., Box 729
Minneapolis, Minnesota 55455
Investigator: John Nyman, Ph.D.

The purpose of this task is to study urban and rural differences in HHA costs, patient characteristics, access to care, and service utilization patterns. The study will be performed in two parts: (1) Costs, patient characteristics, and service utilization patterns will be analyzed using home health care data from the State of Wisconsin. (2) Access to home health care services will be examined with use of patient-level Medicare data. Mathematica Policy Research, Inc., as a subcontractor for this study, will apply two of the "Hospital Aftercare" guidelines (see the project described below) to Medicare plan of

treatment data to develop a measure of access between urban and rural recipients of home health care.

Natural History of Post-Acute Care for Medicare Patients

Period: December 1986-September 1990
Funding: $ 3,373,670
Awardee: University of Minnesota
School of Public Health
420 Delaware Street, S.E.,Box 197
Minneapolis, Minnesota 55455
Investigator: Robert Kane, M.D.

This is a study of the course and outcomes of post-acute care. It has two major components: analysis of Medicare data assess differences in patterns of care across the country and to determine the extent of substitution where various forms of post-acute care services are more or less available, and detailed examination of clinical cases from the most common diagnostic-related groupings receiving post-acute care in a few selected locations. Measure of the complexity of the clinical cases will be developed using a modification of the medical illness severity grouping system. This project is jointly funded with the Office of the Assistant Secretary for Planning and Evaluation.

Data collection is continuing. A report of the findings from the analysis of national Medicare data will be published late in 1989. This project is analyzing preliminary data in order to address questions about the need for and the consequences of providing long-term care to post-hospital patients.

Analysis of Hospital Aftercare Under Prospective Payment

Period: April 1986-October 1989
Funding: $ 1,436,268
Contractor: System Sciences, Inc.
4330 East-West Highway
Bethesda, Maryland 20814
Investigator: Cyrus Baghelai

The purpose of this pilot study was to develop and field test methods for determining the appropriateness of post-discharge aftercare services. Study methods involved classifying patients at the time of their discharge from the hospital according to their post-discharge service needs and applying professionally developed guidelines to project aftercare needs. Projected need was then compared with services received based on interview data.

The project methodologies and instrumentation have been completed and field tested. The final report has been submitted.

Trends in Patterns of Post-Hospital Service Use and Their Impact on Outcomes

Period: June 1987-May 1990
Funding: $ 293,922
Awardee: Duke University
Demographic Studies
2117 Campus Drive
Durham, North Carolina 27706
Investigator: Kenneth Martin, Ph.D.

This project is examining the pattern of care delivered after hospitalization for different types of hospitalized patients, as distinguished by diagnosis, age, sex, and other data elements contained on the Medicare Part A bill. Post-hospital use patterns are examined in terms of types and duration of Medicare services received and the proportion of patients receiving care. Similar patterns will then be examined for non-hospitalized Medicare beneficiaries.

The project has focused on expanding and cleaning data files used in previous analyses.

Prospective Payment Systems and Post-Hospital Care: Use, Cost, and Market Changes

Period: September 1985-September 1989
Funding: $ 706,118
Awardee: Georgetown University
Center for Health Policy Studies
2233 Wisconsin Avenue, N.W.
Washington, D.C. 20007
Investigator: Judith Feder, Ph.D. and William Scanlon, Ph.D.

The purpose of the project is to determine how much the hospital PPS shifts care from the hospital to SNF's and home health providers and to analyze the impact of this shift on total costs to Medicare and on changes in SNF characteristics that are likely to cause an increase in use by Medicare beneficiaries in the future. Medicare claims will be analyzed to determine how PPS has affected total service use (hospital, SNF and home health) and costs for hospital patients. In addition, SNFs will be surveyed to identify changes in nursing home patients, services, and market structure likely to affect Medicare use. The survey will be supplemented with data from the Medicare/Medicaid Automated Certification System (MMACS), SNF cost reports, and other sources.

Major project activities include:

- o Completion of the nursing home survey.
- o Analysis of survey and MMACS data.
- o Initiation of claims analysis.
- o Completion of 1982 and 1985 Medicare claims processing for pre/post-PPS analysis.
- o Completion of a three-stage sampling process of study hospitals.

The final report is expected by the end of 1989.

Changes in the Post-Hospital Care Utilization Among Medicare Patients

Period: August 1989-July 1990
Funding: $ 102,247
Awardee: The Rand Policy Research Center
1700 Main Street
Santa Monica, California 90406
Investigator: Richard Neu, Ph.D.

This project will create a data file linking Medicare billing records for inpatient hospital and post-hospital care during 1987 and 1988. Rand will use this file to document changes in post-hospital utilization among Medicare patients in recent years. The analyses will include an examination of SNF, HHA, and rehabilitative hospital care. This study is in the early developmental stage.

Massachusetts Health Care Panel Study of Elderly - Wave IV

Period: July 1984-January 1990
Funding: $ 152,408
Awardee: Harvard University/Harvard Medical School
1350 Massachusetts Avenue
Holyoke Center 458
Cambridge, Massachusetts 02138
Investigator:

This project collected the fourth wave of self-reported information from the Massachusetts Health Care Panel Study cohort, a group that was selected 10 years as a statewide probability sample of all persons 65 years of age or over. The data from the first three waves were analyzed and the results

have been reported in numerous articles in professional journals. In this project, the data from all four waves are being analyzed to determine markers of functional decline during pre-death, predictors of long-term care institutionalization, and interrelationships between physical, behavioral, and social characteristics and subsequent health care and social service utilization and mortality.

All of the data for this project have been gathered. Analysis of the data is underway, and a final report is expected in 1990.

Cohort Analysis of Disabled Elderly

Period: August 1988-January 1990
Funding: $ 89,986
Awardee: Brandeis University Research Center
415 South Street
Waltham, Massachusetts 02254
(The Urban Institute - subcontractor)
Investigator: Korbin Liu, Sc.D.

The project applies event history analyses to nationally representative data sources to derive estimates of the transitions between various health status categories and the duration within categories for different age groups. These data sources include: Multiple years of National Health Interview Surveys, mortality records of National Long-Term Care Surveys, Longitudinal Study on Aging, and the National Nursing Home Surveys. Researchers assigned to the project will also estimate, based on the type and level of morbidity and disability categories, the risks involved and duration of specific types of acute and long-term care.

To date, many of the key data sets have been formatted for analysis and initial analyses have been conducted. In the coming project year, the analysis employing grade of membership methodology to control for population heterogeneity across the data sets will be completed.

Medicaid Tape-to-Tape: Research Data and Analysis

Period: March 1986-October 1990
Funding: $ 5,141,406
Contractor: SysteMetrics, Inc.
104 West Anapamu Street
Santa Barbara, California 93101
Investigator: Embry Howell

This project continues the development and implementation of

a Medicaid person-level data set from five State Medicaid Management Information Systems (MMIS) (California, Georgia, Michigan, New York, and Tennessee). This effort will acquire data on enrollment, claims, and providers for 1985-88. These data will be used to create uniform files, provide descriptive reports, support analysis and evaluation, and develop methodology for online data base management. This project will provide a continuum of 9 years of uniform Medicaid data for the conduct of analysis of program management, evaluation of policy alternatives, and feedback to States in the area of Medicaid financing.

Currently, project staff are acquiring and processing person-level enrollment, claims, and provider data that have been obtained from State MMIS. Project staff are also linking the data base to other kinds of health statistics to expand the uses of the data. The project will continue to produce early return tabulations that summarize enrollment, utilization, and expenditures data for each year and each participating State. Research is underway on a series of special topics including: capitation in Medicaid, spend down and its relationship to nursing home entry, the chronically mentally ill, hip fractures among the elderly, inpatient hospital use by Medicaid children, hospital reimbursement, Medicaid drug utilization, obstetrical services, physician volume, AIDS and Medicaid providers. The following reports have been published:

- Acquired immunodeficiency syndrome in California's Medicaid Program, (1981-1984),"Health Care Financing Review, Vol. 10, No.1, HCFA Pub. No. 03274, Fall 1988.

- Utilization and Expenditures under Medicaid for Supplemental Security Income Disabled," Health Care Financing Review, Vol. 11,No. 1, HCFA Pub. No. 03286, Fall 1989.

- Prenatal, Delivery, and Infant Care Under Medicaid in Three States," Health Care Financing Review, Vol. 10, No. 4, HCFA, Pub. No. 03284, Summer 1989.

A Longitudinal Study of Case-Mix Outcomes and Resource Use in Nursing Homes

Period:	September 1985-November 1988
Total Funding:	$ 722,135
Awardee:	Brown University Box G Providence, Rhode Island 02912
Investigator:	Vincent Mor, Ph.D.

This study of natural histories of patient outcomes was designed to analyze the variation in outcomes for nursing home residents and the relationship between case-mix adjusters and these outcomes. Using several large administrative data sets, the project focused on quality based outcome measures such as changes in physical function, discharge status, and changes in clinical conditions and the receipt of services. Data on residents from the National Health Corporation, New York State, and Texas facilities were used in these analyses.

The study consisted of three major areas of analyses. The first set of analyses described probabilities of functional change and discharge locations for a cohort of residents newly admitted to the nursing home. Analyses of the changing risk of discharge dead, to home, and to the hospital over the first year of stay show that early in the stay, a positive outcome is strongly related to the functional abilities of the residents. The longer residents remain in the facility, the less likely they are to leave.

Three different data sets were then used to describe the relationship between case-mix adjusters and quality indicators. Outcomes examined include several measures of physical functioning, decubitus ulcers, urinary tract infections, contractures, and the use of restraints and bladder and bowel definitions used, and populations studied, some common patterns were identified. Changes in functional abilities were more consistently associated with age than with diagnosis.

The final phase of analysis was a validation of three multivariate models that predict 6-month outcomes. The models predict functional improvement, functional decline, and death for a cross-section of nursing home residents. Each model was initially developed with data from Rhode Island, as part of a study funded by the National Center for Health Services Research. Using data from New York State and National Health Corporation nursing home residents, these three models were re-estimated. Overall, the majority of terms in the three models were related to the outcomes as found in the Rhode Island models. There was some variation in the magnitude and significance of the relationships. However, robust associations were found for parameters that were most consistently defined and those that were less dependent on variations in practice patterns. Functional status, as measured by the eating and transfer, was the patient characteristic most consistently related to prevalence and incidence of decubitus ulcers, urinary tract infections, contractures, and restraint use.

Several papers based on this research have appeared in the literature. The final report has been received and will be submitted to NTIS.

Community Care for Alzheimer's and Related Diseases

Period:	June 1987-December 1989
Total Funding:	$ 127,970
Awardee:	The Urban Institute 2100 M Street, N.W. Washington, D.C. 20037
Investigator:	Korbin Liu, Sc.D.

The awardee will analyze data from the National Long Term Care Channeling Project (1982-84) to determine the range of services, sources, and costs of care used by community residents with cognitive impairment and to determine the risks of their entering nursing homes, as a function of physical and mental health status, and the types and amounts of care received in the community. The study is expected to provide baseline information for the Alzheimer's disease demonstration project that is congressionally mandated in section 9342 of the Omnibus Budget Reconciliation Act of 1986.

Analyses of several cost centers for community care and risks of nursing home admissions currently are being carried out. In addition, HCFA has approved an additional task that permits an assessment of the feasibility of using a longitudinal data base from the Triage/Connecticut Community Care, Inc. This data base contains details on patient assessment and management systems that may provide additional information on the costs of persons with Alzheimer's disease and related disorders.

Feasibility Analysis for Pathways to Long Term Care Project

Period:	August 1989-November 1989
Funding:	$19,994
Awardee:	Brandeis University Research Center 415 South Street Waltham, Massachusetts 02254
Investigator:	Walter Leutz, Ph.D.

This study will determine the feasibility of analyzing Social/Health Maintenance Organization data on service use that tracks individuals as they make a transition from a state of health to one of severe impairment. If a sufficient amount of data is available, subsequent analysis may be approved with additional funds to determine whether definable "pathways" could be derived. These pathways to long term care could assist in case management practice and provide outcome related information regarding the use of long term care services in a managed care setting.

The feasibility study was completed November 30, 1989. Based on the study, a decision will be made whether or not to fund additional activities.

Activities of Daily Living (ADL) Measurements as Determinants of Eligibility

Period:	August 1989-May 1990
Funding:	$99,991
Awardee:	Brandeis University Research Center 415 South Street Waltham, Massachusetts 02254
Investigators:	John Capitman, Ph.D. and Korbin Lui, Sc.D.

The study will use the National Long Term Care Survey, Channeling data and the Social Health Maintenance Organizations' Comprehensive Assessment Form data to examine issues associated with defining and measuring ADLs for use as eligibility criteria. A cost analysis will be performed and other issues associated with using ADL scores as eligibility criteria for Medicare services, will be discussed.

Among the questions to be addressed are:

- What level of ADL impairments is used to trigger eligibility?
- Which ADL items should be used?
- Under what circumstances should assessments be performed, and by whom?

The study is in the early developmental stage.

Study of Adult Daycare Services

Period:	June 1989-January 1990
Funding:	$93,750
Awardee:	University of California at San Francisco
Investigator:	Rick Zawadski, Ph.D.

Section 208 of the (now repealed) Medicare Catastrophic Coverage Act of 1988 mandated an updated survey of adult day centers. The legislation requests that this survey provide information on: 1) who is served by adult day centers; 2) how many centers are there and where are they located; 3) what services do they provide; 4) what are the characteristics of operating these centers; 5) who now funds these centers; 6) what is the cost of operating these centers; 7) are there licensing, certification, and quality assurance standards governing these centers; and 8) how do these characteristics vary by State.

An initial 1985 survey was performed by the National Institute of Adult Daycare (NIAD), a constituent unit of the National Council on the Aging, with the assistance of a few adult day center consultants.

Status: Funding for the survey was obtained from the American Association for Retired Persons. All the known and designated adult day centers in the United States were mailed a survey during February 1989. A contract was awarded to the University of California at San Francisco to perform the analyses of the survey data. Both Congressional reports are anticipated for completion by June 1990.

Long Term Care Studies

Period: September 1989-September 1994
Funding: $ 3,790,234
Awardee: Health and Sciences Research Incorporated
Investigator: David Kennell, Ph.D.

This project will conduct research related to the delivery and financing of long term care services for Medicare beneficiaries. The project will focus on four major areas:

1) the financial characteristics of Medicare beneficiaries who receive or need long term care services;
2) how the characteristics of Medicare beneficiaries affect their utilization of institutional and non-institutional long term care services;
3) how relatives of Medicare beneficiaries are affected financially and in other ways because the beneficiaries require or receive long term care services; and
4) how the provision of long term care services may reduce expenditures for acute health care services.

Analyses will use existing long term care and other survey data bases, such as the National Long Term Care Surveys, the Longitudinal Study of Aging, the National Nursing Home Survey, the Survey of Income and Program Participation and the National Medical Care Expenditure Survey. Medicare administrative records and other extant information will also be utilized. Three reports are required under the contract. The project was awarded on September 29, 1989. The first report is scheduled for December 1990.

Goals and Strategies for Financing Long Term Care

Period: August 1989-March 1990
Funding: $95,409
Awardee: University of Minnesota Research Center
420 Delaware Street, S.E., Box 729
Minneapolis, Minnesota 55455
Investigator Mark Pauly, Ph.D.

The purpose of this project is to use concepts drawn from a number of disciplines - economics, decision sciences, policy analysis, sociology, and demography - to develop statements of possible objectives for long term care insurance. Defining objectives will

include an analysis of benefits and costs from potential changes in financing and an analysis of expected behavioral changes in response to changes in financing. The meaning of these objectives will then be illustrated by applying them to several different types of policy proposals:

- Subsidization of private insurance;
- Employer-provided insurance;
- "Whole-life" versions of insurance;
- Means tested public insurance;
- "Medicaid-equivalent" subsidies;
- "Catastrophic" public insurance; and
- Public provision of information on Medicare coverage and the need for insurance.

The study is in the early developmental stage.

Long Term Care Supply and Medicare Hospital Utilization

Period: August 1989-March 1990
Funding: $ 47,986
Awardee: Abt Associates, Inc.
55 Wheeler Street
Cambridge, Massachusetts 02115
Robert Schmitz, Ph.D.

The purpose of this project is to investigate how local variations in the availability of nursing home beds affect Medicare rates of hospitalization. Effects on the number of admissions, the number of hospital readmissions, the number of hospital days used, and the costs per Medicare Part A enrollee are to be evaluated. Urban-rural differences will be assessed. The impact of community long term care services, Medicare risk contract Health Maintenance Organization services and the Prospective Payment System upon Medicare Part A utilization are to also be evaluated. The study is in the early developmental stage.

PACE (On Lok) Case Study

Period: August 1989-January 1991
Funding: $ 172,138
Awardee: University of Minnesota Research Center
420 Delaware Street, S.E., Box 729
Minneapolis, Minnesota 55455
Investigator: Robert L. Kane, M.D.

This study will provide a descriptive analysis of the elderly stages of the Program for All-inclusive Care for the Elderly (PACE) demonstration. The study will examine in detail the model of delivery provided by On Lok Senior Health Services, San Francisco, California, and the degree to which aspects of this model are successfully replicated in as many as eight sites nationwide through guided interviews, site visit observations, and review of

written materials pertaining to site development and operations. The results of the study are expected to have utility as subsequentsites are developed for later implementation. The study is in the initial design phase. Initial site visits to On Lok and PACE sites are scheduled for late 1989.

Analysis of State Systems for Providing Intermediate Care Facility for the Mentally Retarded and Other Care for the Mentally Retarded

Period: June 1987-May 1989
Funding: $ 88,268
Awardee: Center for Residential and Community Services
University of Minnesota
150 Pillsbury Drive, S.E.
Minneapolis, Minnesota 55455
Investigator: Charles Lakin, Ph.D.

This project updated information on the status of and changes in residential services for the mentally retarded gathered by this awardee for 1977 and 1982 in a previous HCFA-funded grant. Data on the current status of the intermediate care facility for the mentally retarded (ICF/MR) program, which were obtained through the Inventory of Long Term Care Places, the sampling frame for the institutional component of the National Medical Expenditures Survey, were analyzed and supplemented by case studies of selected State's programs for serving the mentally retarded.

This project analyzed data from the tape of the Inventory of Long Term Care Places and conducted in-depth State studies. A final report was received in May 1989 and is entitled "Medicaid Services for Persons with Mental Retardation and Related Conditions." It is available from the NTIS. Study results show that community-based services have become the primary model of care for persons with mental retardation and related conditions. Conversely, the ICF/MR program has shown little growth in the recent past and the numbers of persons served by this program have decreased in a majority of states. These facts, as well as the wide acceptance of the Home and Community-Based Services waiver, indicate the need to begin viewing the services system for persons with mental retardation as a community-based, rather than an institutionally-based system.

Long Term Care: Elderly Service Use and Trends

Period: August 1989-August 1990
Funding: $245,249
Awardee: The Brookings Institution
175 Massachusetts Avenue, N.W.
Washington, D.C. 20036-2188
Investigator:

This project has three objectives: (1) an analysis of the financial status of nursing home users; (2) an analysis of the determinants of home care use; and (3) projections of the numbers and level of disability among the elderly and their use of long term care services. Data from the following major surveys will be used: 1982 - 1984 National Long Term Care Surveys: The 1984 - 1986 Supplement on Aging/Longitudinal Study of Aging; and the 1984 Survey of Income and Program Participation. Data will be analyzed using cross-tabulations and logistic and Least squares regression analyses and the Brookings/ICF simulation model (updated and revised). The project has just begun. Analytical data files are being developed.

Analysis of Long Term Care Payment Systems

Period: April 1983-December 1988
Funding: $ 1,394,293
Awardee: Center for Health Services Research
University of Colorado
1355 South Colorado Boulevard
Suite 706
Denver, Colorado 80222
Investigator: Robert Schlenker, Ph.D.

This project is a comparative analysis of long term care reimbursement systems in seven States (Colorado, Florida, Maryland, Ohio, Texas, Utah, and West Virginia). The study will combine an empirical analysis of nursing home costs and payments and the determinants of costs with a detailed qualitative analysis of the operations of the reimbursement systems.

The comparative analysis across States will be performed through a unique "comparison-by-substitution" method that assesses reimbursement for nursing homes in one State under the assumption that the other States' reimbursement systems are in effect. Data sources for this study include primary facility information and patient samples, as well as secondary sources such as cost reports.

Major project activities include:

Volume 1: A Multi-State Analysis of Medicaid Nursing Home Payment Systems, December 1988.

Volume 2: Administering Nursing Home Case Mix Reimbursement Systems: Issues of Assessment, Quality, Access, Equity and Cost, December 1988.

Volume 3: Analyzing Nursing Home Capital Reimbursement Systems, December 1988.

Evaluation of "Life-Continuum of Care" Residential Centers in the United States

Period: January 1985-September 1989
Funding: $ 832,871
Awardee: Hebrew Rehabilitation Center for the Aged
1200 Centre Street
Boston, Massachusetts 02131
Investigator: Sylvia Sherwood, Ph.D.

The objective of this 3-year project is to obtain information about the characteristics of continuum of care residential center (CCRC) facilities and their residents and compare them with elderly residents living in the community, with respect to quality of life and health, service costs, and utilization. Data will be gathered from 20 CCRCs in four areas: California, Arizona, Florida, and Pennsylvania. These sites will be stratified according to the type of contract offered (extended versus limited), the age of the facility, and the income level of those enrolled. Three types of CCRC residents will be selected from the sites for the study sample: new admissions (580), existing residents, both short- and long-stay residents (1,640), and residents who died just prior to or during the field data gathering period (660). Quality of life and service utilization data will be gathered at two points in time, at baseline and 12 months later. Three types of comparison samples will be employed:

- A representative sample of elderly in their own homes or independent apartments (2,422).
- A national sample of elderly living in congregate housing settings (2,350).
- A representative sample of elderly who have died and for whom retrospective data are available for their last year of life (1,500).

The final report is expected by the end of 1989.

Financial Impact to Beneficiaries of Nursing Home Care

Period: August 1988-February 1990
Funding: $ 129,888
Awardee: Brandeis University Research Center
415 South Street
Waltham, Massachusetts 02254
Investigator: Korbin Liu, Sc.D.

This project will use the Urban Institute's Transfer Income Model (TRIM)-2 for State estimates and the Connecticut Nursing Home Inventory data base to calculate nursing home use and payments. The TRIM-2 model is a microsimulation model, based on the 1984 Current Population Survey, used in forecasting use and payments. The Connecticut Inventory data base contains patient-specific information on all nursing home patients (private and public) from 1977 to the present. In addition, the 1985 National Nursing Home Survey will be used to analyze several dimensions of nursing home use. From the collected data, estimates will also be made for the nursing home patients' spend-down provision.

A report entitled "Changes in Duration and Outcomes of Nursing Home Stays: 1977 - 1985" was completed. The report concludes that changes have occurred in the overall composition of nursing home admissions in the intervening 8 years between 1977 and 1985. The analysis of changes between 1977 and 1985 among nursing home admissions indicates that the nursing home patients had become older, more disabled, and more likely to have been admitted for terminal care. This conclusion is reflected by the shorter length of stay for the total cohort of nursing home admissions, the increase in mortality outcomes at discharge, particularly for persons with short stays (e.g., less than 30 days), and the disability characteristics of patients at admission.

Reasons for the changes in the composition of nursing home admissions are not as clear as the occurrence of the changes themselves. One possibility is that the relatively slow growth of nursing home beds between 1977 and 1985 relative, for example, to the 8 years before 1977, has resulted in a selection process whereby the most disabled persons are being admitted. Another possible reason is the change in acute care utilization that occurred between 1977 and 1985. Although many changes were occurring, the most widely known was Medicare's hospital PPS, which provided strong incentives for hospitals to discharge patients as quickly as possible. As a result, the use of nursing homes to substitute for the tail end of hospital stays was widely expected. Study findings that greater proportions of short-stay patients (i.e., less than 30 days) were discharged dead or to a hospital in 1985 relative to 1977 is consistent with the theory that greater use of nursing homes for post-acute care was a direct result of the hospital PPS policy.

During the coming year, the project will complete:

(1) Development and analysis of a synthetic cohort of nursing home admissions with data from the Connecticut nursing home inventory.

(2) Estimation of spenddown rates and numbers of persons at the State level through the use of the TRIM model.

Can Geriatric Nurse Practitioners Improve Nursing Home Care?

Period: September 1983-December 1988
Funding: $ 673,759
Awardee: The Rand Corporation
1700 Main Street
Santa Monica, California 90406
Investigator: Joan Buchanan, Ph.D.

The purpose of the study is to evaluate the potential of the use of geriatric nurse practitioners for improving outcomes of care and containing costs in SNFs. The 30 nursing homes that participated in the Mountain States Health Corporation (MSHC) geriatric nurse practitioner (GNP) demonstration project were compared with 30 nursing homes in the region that did not participate. Comparisons were made of:

- Patient outcomes.
- Process of care.
- Nursing home costs.
- History of certification deficiencies.

Homes were matched by State, ownership, bed size, and urban, suburban, or rural location.

Study findings indicated that the MSHC GNP program had a limited positive effect. If the employment market for nurses remains unchanged, the program will prove relatively inexpensive to implement, especially in larger facilities. Nor did the program adversely affect nursing home per diem costs or profits. Further it would appear that GNPs decreased hospital use for patients newly admitted to nursing homes.

The following publications are available:

1. The Financial Impact of Nursing Home-Based Geriatric Nurse Practitioners: An evaluation of the Mountain States Health Corporation GNP Project," Santa Monica, California: The Rand Corporation, Report #R-3694-HCFA/RWJ, May 1989.

2. "Geriatric Nurse Practitioners as Nursing Home Employees: Implementing the Role" Gerontologist 28(4), 1988.

3. "Effects of a Geriatric Nurse Practitioner on Process and Outcome of Nursing Home Care" AJPH 79(9), September 1989.

Analysis of Long Term Care Payment Systems

Period:	April 1983-December 1988
Funding:	$ 1,394,293
Award:	Cooperative Agreement
Awardee:	Center for Health Services Research University of Colorado 1355 South Colorado Boulevard, Denver, Colorado 80222
Investigator:	Robert Schlenker, Ph.D.

This project conducted a comparative analysis of long term care reimbursement systems in seven States (Colorado, Florida, Maryland, Ohio, Texas, Utah, and West Virginia). The study combined an empirical analysis of nursing home costs and payments and the determinants of costs with a detailed qualitative analysis of the operations of the reimbursement systems. The comparative analysis across States was performed through a unique "comparison-by-substitution" method that calculated reimbursement for nursing homes in one State under the assumption that the other States' reimbursement systems were in effect. Data sources for this study included primary facility information and patient samples, as well as secondary sources such as cost reports.

The final report is available in three volumes:

Volume I: A Multi-State Analysis of Medicaid Nursing Home Payment Systems, December 1988.

Volume II: Administering Nursing Home Case Mix Reimbursement Systems: Issues of Assessment, Quality, Access, Equity and Cost, December 1988.

Volume III: Analyzing Nursing Home Capital Reimbursement Systems, December 1988.

Additional reports are also available:

- "Case-Mix Measures and Medicaid Nursing Home Payment-Rate Determination in West Virginia, Ohio, and Maryland," March 1984.
- "Overview of Medicaid Nursing Home Reimbursement Systems," March 1984.
- "Case-Mix and Capital Innovations in Nursing Home Reimbursement," August 1984.
- "An Analysis of Long Term Care Payment Systems: Research Design," October 1984.
- "The Long Term Care Policy Environment in Seven States," May 1985.
- "Medicaid and Non-Medicaid Case-Mix Differences in Colorado Nursing Homes," September 1985.
- "Case-Mix Reimbursement for Nursing Home Services: A Three-State Simulation Model," October 1985.
- "Case Mix in Connecticut Nursing Homes: Medicaid Versus Non-Medicaid, Profit Versus Non-Profit, and Urban Versus Rural Patient Groups," December 1985.
- "Analyzing Nursing Home Profits," May 1986.
- "Case-Mix Reimbursement for Colorado Nursing Homes."

Prevention of Falls in the Elderly

Period: September 1984-December 1989
Total Funding: $ 695,894
Awardee: Kaiser Foundation Research Institute
Health Services Research Center
4610 Southeast Belmont Street
Portland, Oregon 97215
Investigator: Mark Hornbrook, Ph.D.

In September 1984, a cooperative agreement was awarded to the Kaiser Foundation Research Institute to test both the cost-effectiveness of a comprehensive environmental and behavioral program designed to prevent falls in the elderly and to estimate the net financial benefits or costs to a health maintenance organization and the Medicare program of a given level of falls prevention for a defined target population. Funding support for this demonstration was supplemented by the National Institute on Aging, the Robert Wood Johnson Foundation, and Kaiser Foundation Hospitals, Inc. The project was conducted at the Health Services Center, Kaiser Permanente Medical Care Program in Portland, Oregon. This was a randomized study of 2,509 households with one or more Kaiser members aged 65 or over who were recruited into two groups, control and intervention. Baseline data on household environmental circumstances and fall hazards and the member's physical and psychological health status were obtained during a home audit. Participants were randomized into one of the two groups. Participants in the intervention group were offered a special falls prevention program that included a self-management educational curriculum and the installation of safety equipment and minor home renovations to correct safety hazards. In addition, a retrospective medical record review will be completed for a blind control group consisting of a 5 percent sample of Kaiser members age 65 and over to measure the incidence of falls-related medical care use.

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The project is in its fifth year of operation. The follow-up period to assess the incidence of falls ended December 1987. The cooperative agreement was extended until December 1989 to allow completion of the evaluation of the program's effectiveness in lowering the frequency and severity of falls and to determine whether the program is cost-effective (i.e., whether the cost of the intervention is offset by the savings in medical costs associated with the prevented falls). The final report is expected by the spring of 1990.

Modifications of the Texas System of Care for the Elderly: Alternatives to the Institutionalized Aged

Period: January 1980-June 1990
Total Funding: Waivers only
Grantee: Texas Department of Human Resources
701 West 51st Street
P.O. Box 2960
Austin, Texas 78769
Investigator: Kent Gummerman, Ph.D.

The purpose of this project is to reduce the growth of nursing homes in Texas and, at the same time, expand access to community care services for needy Medicaid individuals. It is being accomplished by directly changing the operating policies of the State's title XIX and title XX programs -- specifically, by eliminating the State's lowest level of institutional care, ICF-II. Existing organizations responsible for the State's title XIX and title XX programs are responsible for project implementation.

Substantial progress has been made in achieving project objectives. In March 1980, there were 15,486 individuals in the ICF-II group. As of December 1988, there were 506 ICF-II clients remaining. From March 1980 to December 1988, the total institutional population also decreased from 64,820 to 54,365 clients (a reduction of 16.1 percent), while the community-care population has grown from 30,792 to 46,958 -- an increase of slightly more than 52 percent. This project was scheduled to terminate on December 31, 1989, but a 6-month extension (through June 1990) is required by the 1989 budget reconciliation legislation.

The Medicare Alzheimer's Disease Demonstration

Period: September 1989-September 1993
Funding: $1,999,812
Awardee: Institute for Health and Aging
University of California San Francisco
210 Filbert Street
San Francisco, California 94133
Investigator: Robert Newcomer, Ph.D.

Section 9342 of P.L. 99-509, the Omnibus Budget Reconciliation Act of 1986, directed the Secretary to conduct demonstration projects to determine the effectiveness, cost, and impact of providing comprehensive services to Medicare beneficiaries who are victims of Alzheimer's disease or related disorders. The legislation specified that the project shall be conducted over a period of 3 years, and that sites must be geographically diverse, located in States with a high proportion of Medicare beneficiaries, and in areas readily accessible to a significant number of beneficiaries. The legislation authorized the expenditure of up to $40 million from the Medicare Part B Trust Fund for the demonstration.

HCFA was assisted in designing and implementing the demonstration during the period September 1987 through June 1989 by Mathematica Policy Research, Inc., under a contract with HCFA. Two models of care are being studied under this project. Both provide case management, homemaker/personal care services, adult day care, and education and counseling for family caregivers. Case management activities include assessment, care planning, service arrangement, and patient monitoring. The two models vary by their monthly expenditure caps and the intensity of their case management. Eight demonstration sites were selected through a competitive process during 1988. The demonstration sites are:

Monroe County Long Term Care Program, Inc.
Rochester, New York

Carle Clinic
Urbana, Illinois

Northeast Community Mental Health Center
Memphis, Tennessee

Good Samaritan Hospital and Medical Center
Portland, Oregon

Cincinnati Area Senior Services, Inc.
Cincinnati, Ohio

Wood County Senior Citizens Association
Parkersburg, West Virginia

The Wilder Foundation
Minneapolis, Minnesota

Miami Jewish Home and Hospital
Miami, Florida

After an initial site planning and development period that began in May 1989, the demonstration sites began furnishing services to clients in December 1989. The sites are expected to serve more than 2,000 clients during the demonstration, with an equal number of eligible individual assigned to a control group.

In September 1989, HCFA awarded this contract to the University of California San Francisco to perform an independent evaluation of the demonstration and to provide training and technical assistance to the sites.

New Jersey Respite Care Pilot Project

Period: July 1988-September 1990
Total Funding: Waivers only
Grantee: New Jersey Department of Human Services
222 South Warren Street
Trenton, New Jersey 08625
Investigator: William Ditto

The New Jersey Respite Care Pilot Project was implemented in 1988 to help individuals care for elderly and disabled family members who are at risk of institutionalization by providing services and support needed by both care-recipients and caregivers. The purpose of the study is to determine the extent to which the provision of respite care services will delay or avert institutional placement and enhance and sustain the role of the family in providing long term care services. All of New Jersey's 21 counties are participating in the program. The respite care services provided under this project include short-term and intermittent companion services; homemaker, home health aides, and personal care services; adult day care; and inpatient respite in a hospital or nursing home. Services are available on a planned or emergency basis. In addition to these services, peer support, training, and counseling is provided to family caregivers.

HCFA originally was directed to approve this project by the Omnibus Budget Reconciliation Act of 1986. New Jersey did not implement the project after the passage of the original authorizing legislation because of a provision that required all participants to be Medicaid-eligible. The project's eligibility criteria were later amended by the Omnibus Budget Reconciliation Act of 1987 to provide authorization for the program to include a non-Medicaid population, and the program began on July 1, 1988. During its first year, respite care services were provided to over 1,000 elderly or disabled clients and their families. The project is scheduled to end in September 1990.

In compliance with one of the requirements of the legislation, the State has arranged for an independent evaluation of the project to be conducted by the Center for Health Policy and Aging Research at Rutgers University. The final report is expected in early 1991.

HHA Prospective Payment Demonstration

Period: December 1983-December 1989
Total Funding: $ 2,839,501
Contractor: Abt Associates, Inc.
55 Wheeler Street
Boston, Massachusetts 06115
Investigator: Henry Goldberg

The purpose of this project is to develop and test alternative methods of paying HHAs on a prospective basis for services furnished under the Medicare program. The demonstration will enable HCFA to evaluate the effects of various methods of prospective payment on health care expenditures, quality of home health care, and home health agency operations.

In response to section 4027 of the Omnibus Budget Reconciliation Act of 1987, which directs HCFA to conduct a demonstration of prospective payment for HHA, Abt Associates is working with HCFA to develop a project design and to assist HCFA in implementing the demonstration. At this time, HCFA and Abt are finalizing details of the proposed payment methods that will be tested. As part of this effort, Abt is also performing analysis of HHA plans of treatment, cost reports, and Medicare claims to provide HCFA with information about length of home health episodes and the relationship between patient characteristics and resource use. The operations phase of the demonstration is expected to begin in mid-1989.

The demonstration will test two prospective payment approaches - payments per visit by type of discipline and payments per episode of Medicare-covered home health care. Each HHA's payment rates will be based on its own Medicare allowable costs in the 12-month period prior to the HHA entering the demonstration. The study design calls for recruitment of 100 HHAs from five States (California, Florida, Illinois, Massachusetts, Texas) to participate voluntary in the demonstration. HHAs that agree to participate in the demonstration will be randomly assigned to one of three groups - i.e., to one of the two payment methods or to a control group that continues to be reimbursed in accordance with the current retrospective cost system. In order to assure that the incentives of prospective payment do not lead to reductions

in the quality of home health care or in access to necessary and appropriate services, Peer Review Organizations in the five demonstration States will conduct ongoing quality assurance reviews of a sample of patient records from the participating HHAs. HCFA will award a contract in 1990 for an independent evaluation of the demonstration.

Design of a Demonstration of Medicare Payment for Community Nursing Organizations

Period: August 1988-December 1989
Total Funding: $ 196,109
Awardee The People-to-People Health Foundation
(Project HOPE)
2 Wisconsin Circle, Suite 500
Chevy Chase, Maryland 20815
Investigator: Burton Dunlop, Ph.D.

Section 4079 of the Omnibus Budget Reconciliation Act of 1987 directs the Secretary to conduct a demonstration testing Medicare reimbursement on a capitated basis for services furnished by Community Nursing Organizations (CNOs). Project HOPE is assisting HCFA with the design of the demonstration. Tasks involved in this development effort include developing the eligibility standards for CNOs, the methodology for calculating the capitated payment rates, a research design and evaluation strategy for the demonstration, site selection criteria, quality assurance mechanisms, and marketing strategies for the sites. Development activities are still underway. Implementation of the demonstration will begin in 1990 after completion of these activities.

Prior and Concurrent Authorization Demonstrations

Period: September 1987-July 1992
Total Funding: $598,000
Contractor: Lewin/ICF
1090 Vermont Ave.
Washington, D.C. 20005
Investigator: Barbara Manard, Ph.D.

Section 9305 of P.L. 99-509, the Omnibus Budget Reconciliation Act of 1986, requires the Secretary of Health and Human Services to conduct demonstration projects concerning prior and concurrent authorization for post-hospital extended care services and home health services furnished under Part A or Part B of title XVIII. This legislation responds to concerns expressed by HHAs and SNFs that under the current system of Medicare payment they cannot adequately predict what services Medicare fiscal intermediaries

(FIs) will deny as non-covered. It is hypothesized that prior authorization and concurrent authorization payment approaches will reduce the number of services denied without increasing Medicare expenditures. Under prior authorization, providers submit treatment plans to FI's for review prior to the start of care; under concurrent authorization, plans of treatment are submitted when care begins. In both approaches, the provider receives notification from the FI about how many services will be covered. This provides greater certainty about coverage and payment before most services are given. The law required an evaluation of the demonstrations that must address impacts on (1) administrative and program cost; (2) access and availability of post-hospital services and timeliness of hospital discharges; and (3) the accuracy and cost savings of payment determinations and rates of claims denials compared with the current system.

In July 1987, HCFA implemented home health concurrent authorization pilot projects in Illinois and in all States in HCFA's Region VII (Dallas). Lewin/ICF conducted an evaluation of this pilot project; the evaluation was completed in 1989 and a report describing the results was submitted to HCFA. HCFA has prepared a draft Report to Congress based on this report. Lewin/ICF also designed and implemented a separate demonstration of prior and concurrent authorization for SNF services. This demonstration began operations in September 1989. Lewin/ICF will perform an evaluation of this project as well.

Social Health Maintenance Organization

Period:	September 1985-November 1990
Total Funding:	$ 3,547,934
Contractor:	University of California San Francisco Aging Health Policy Center San Francisco, California 94143
Investigator:	Robert Newcomer, Ph.D. and Charlene Harrington, Ph.D.

The social health maintenance organization (S/HMO) seeks to enroll, voluntarily, persons 65 years of age or over in an innovative prepaid program that integrates medical, social, and long term care delivery systems. The S/HMO merges the health maintenance organization concepts of capitation financing and provider risk-sharing developed by HCFA under its Medicare capitation and competition demonstrations with the case management and support services concepts underlying Department of Health and Human Services (DHHS)- sponsored long term care demonstrations serving the chronically ill aged. Evaluation results will be used by HCFA and DHHS to assess whether the S/HMO concept should be

fostered through changes in prepaid Medicare contracting regulations.

This contract was awarded in September 1985. An interim report was forwarded to Congress August 15, 1988. The data collection phase has been completed. Data analysis will be completed, and the final report written by November 1990.

Design, Implementation, and Evaluation of a Prospective Case-Mix System for Nursing Homes in Massachusetts

Period: August 1986-December 1989
Total Funding: $ 362,312
Awardee: Massachusetts Department of Public Welfare
Medical Assistance Division
600 Washington Street
Boston, Massachusetts 02116
Investigator: Susan Flanagan, M.P.H.

This project will design, implement, and evaluate a prospective case-mix system for a random sample of nursing homes in Massachusetts. This payment system will develop and test incentives for these nursing homes to admit and treat heavy-care patients while minimizing declines in quality of care. Experimental facilities will be compared with facilities that will continue to be reimbursed under the present system. A minimum of 18 experimental and 16 control homes will participate. The system will modify four of seven components of the nursing home reimbursement system currently used in the State. For demonstration facilities, nursing services payment will be case-mix adjusted using "management minutes." Incentives to admit and treat heavy-care patients will be used to further modify the nursing cost center. Various financial incentives will also be used to reduce other "controllable" operating costs.

The cooperative agreement was awarded in August 1986. During the first 2 years, project staff finalized aspects of the proposed payment system, assigned volunteer nursing homes to the experimental and control groups, and improved their quality-assurance mechanisms. Implementation of the case-mix system commenced on October 3, 1988 for 1 experimental year. Development of quality assurance indicators using this case-mix data base is in progress during the implementation year. Statewide implementation will be evaluated based on the demonstration results. The demonstration ends December 31, 1989. Evaluation of the demonstration will begin January 1990. A final report is expected in November 1990.

Texas Nursing Home Case-Mix Demonstration

Period: September 1987-September 1991
Total Funding: $ 371,873
Awardee: State of Texas Department of Human Services
P.O. Box 2960 (MC-234-E)
Austin, Texas 78769
Investigator: Pam Coleman

The Texas Department of Human Services will conduct a 3-year demonstration to implement and evaluate a prospective case-mix payment system. The payment system is based on a HCFA-sponsored feasibility study. The major Medicaid objectives of the project are: to match payment rates to resident need; to promote the admission of heavy-care patients to nursing homes; to provide incentives to improve quality of care; to improve management practices; and to demonstrate administrative feasibility of the new system. The objective for Medicare is the development and pilot testing of the administrative processes for implementing Medicare PPS based on a resource utilization group (RUG) system in coordination with Medicaid case-mix systems.

The State will use a quasi-experimental design for the Medicare pilot test to compare the effect of introducing case-mix payment in an experimental catchment area versus continuing the cost-based system in a control catchment area. The State will use a pre-post design for the Medicaid system. The case-mix methodology is based on a review of six different methods in which the New York RUG's II system explained the greatest variance of resource use. The proposed case-mix index has major elements of the RUG's II system and some of the system used in Minnesota. The Texas Index of Level of Effort (TILE) uses four clinical groups to form clusters and develops sub-groups using an ADL scale. The index that will be used for the classification of Medicare patients is the RUG-T18 developed by Brant Fries and Don Schneider. RUG-T18 uses the same clinical groups and ADL scale that are used in the New York RUGs-II system. The difference occurs in the expanded rehabilitation groups for Medicare patients. Two third-party evaluations will be used, one of data reliability and a second of the validity of their data analyses methods.

During the first year, the TILE and RUG-T18 indexes have been reviewed for compatibility. The RUG-T18 classification was reviewed and operationalized to match the HCFA Medicare coverage guidelines published in 1987. Cost analysis of both national and

State samples of Medicareproviders were performed to arrive at baseline costs for calculating the rates for the RUG-T18 groups.

The Texas client assessment, review, and evaluation instrument has been reviewed and revised. It was pilot tested in the Austin area and achieved a high reliability score on case-mix variables. This instrument contains all the rate setting variables for both Medicare and Medicaid. The Texas utilization review process will expand to include more frequent reviews for new admissions, prior authorizations of Medicare stays, classification of individual patients into RUG-T18 groups. The Medicaid payment system became operational in April 1989 and the Medicare demonstration is scheduled to begin in April 1990.

Case-Managed Medical Care for Nursing Home Patients

Period: July 1983-March 1990
Grantee: Massachusetts Department of Public Welfare
180 Tremont Street
Boston, Massachusetts 02111
Investigator: Lois Simon

HCFA granted Medicare and Medicaid waivers to the Massachusetts Department of Public Welfare to permit fee-for-service reimbursement for the provision of medical services by physician-supervised nurse practitioners/physician assistants (NP/PA) for residents of nursing homes. This permits increased medical monitoring that is expected to generate cost savings as a result of fewer hospital admissions and outpatient visits. Providers are responsible for managing and monitoring the health care and medical condition of all enrollees to assure that the primary care needs of nursing home patients are met in a timely fashion, often without resorting to the hospital emergency room. Initial physical exams, medical evaluation, and re-evaluations are being performed by the NP/PA in the nursing home. The NP/PA operates under written protocols that describe the common medical problems to be encountered and appropriate evaluation and treatment procedures. The supervising physician reviews and countersigns the NP/PA's evaluation and prescriptions. The physician is also consulted in any unusual situation or emergency.

The Rand Corporation, as part of the Research Center Cooperative Agreement with HCFA, is evaluating this project, focusing on the project's impact on the use and cost of nursing home and hospital services. This evaluation relies primarily on Medicare and Medicaid claims data. The Pew Foundation has awarded a grant to the University of Minnesota to assess the project's impact on quality of care. Section 9413 of Public Law 99-509, the Omnibus

Budget Reconciliation Act of 1986, mandated the continuation of this project. Section 6114 of the Ominibus Budget Reconciliation Act of 1989 will provide Medicare coverage of this type of service effectivive April 1990.

On Lok's Risk-Based Community Care Organization for Dependent Adults

Period: November 1983-Indefinitely
Grantees: On Lok Senior Health Services
1441 Powell Street
San Francisco, California 94133

California Department of Health Services
714-744 P Street
Sacramento, California 95814
Investigator: Marie Louise Ansak

In response to the congressional mandate of section 603(c)(1) and (2) of Public Law 98-21, the Social Security Amendments of 1983, HCFA granted Medicare waivers to the On Lok Senior Health Services and Medicaid waivers to the California Department of Health Services. Together these waivers permit On Lok to implement an at-risk, capitated payment demonstration in which more than 300 frail elderly persons, certified by the Department of Health Services for institutionalization in a SNF, are provided a comprehensive array of health and health-related services in the community. The current demonstration maintains On Lok's comprehensive community-based program but has modified its financial base and reimbursement mechanism. All services are paid for by a predetermined capitated rate from both Medicare and Medicaid (Medi-Cal). The Medicare rate is based on the average per capita cost for the San Francisco County Medicare population. The Medi-Cal rate is based on the State's computation of current costs for similar Medi-Cal recipients using the formula for prepaid health plans. Individual participants may be required to make copayments, spend-down income, or divest assets, based on their financial status and eligibility for either or both of the programs. On Lok has accepted total risk beyond the capitated rates of both Medicare and Medi-Cal with the exception of the Medicare payment for end stage renal disease. The demonstration provides service funding only under the waivers. The research and development activities are funded through private foundations.

Section 9220 of the Consolidated Omnibus Budget Reconciliation Act of 1985 has extended On Lok's Risk-Based Community Care Organization for Dependent Adults indefinitely, subject to the terms and conditions in effect as of July 1, 1985, except that

requirements relating to data collection and evaluation do not apply.

The Use of Medicaid Reimbursement Data in the Nursing Home Quality Assurance Process

Period: June 1988 - June 1990
Total Funding: $132,930.00
Awardee: Center for Health Systems Research and Analysis
University of Wisconsin-Madison
Room 300 Infirmary, 1300 University Avenue
Madison, Wisconsin 53706
Investigator: David Zimmerman, Ph.D.

The purpose of this project is to assess the feasibility of using Medicaid reimbursement data to target facilities and residents in the nursing home quality assurance survey process. Medicaid reimbursement data appear to hold considerable promise in helping target facilities for more intensive review, identifying specific care areas where deficient care may be present, and identifying individual residents for more detailed review. Information on medication use, sentinal health events, and other indicators can be provided to surveyors in preparation for the field survey. The information can also be used to determine whether problems have recurred after the survey and follow-up visits.

The objectives of the project are: (1) to convert reimbursement data into specific Quality of Care Indicators (QCIs), particularly with respect to drug related measures and medical outcomes; (2) to identify the conditions, standards, and elements in the Federal regulations for which the use of QCIs has the greatest potential benefit; (3) to develop and demonstrate in one State (Wisconsin) the procedures for providing QCIs to survey staffs; (4) to assess the potential for implementing the system in other States; (5) to determine the implications of the proposed HCFA nursing home regulations and the 1987 Omnibus Budget Reconciliation Act provisions for the use of reimbursement data in the quality assurance process; and (6) to design an expanded demonstration of the use of QCIs in the survey process.

Fifteen preliminary QCIs have been developed and are currently being reviewed by project staff and the advisory panel. The QCIs have been linked to specific conditions, standards, and elements within the existing Federal regulations, and proposed new regulations are being reviewed to determine their relationship with the QCIs. Deficiencies and QCIs in Wisconsin for the period August 1987-1988 are being analyzed to determine the baseline relationship between the two measures. Preliminary discussions

with survey staff have been held to develop the system for conveying QCI information to the surveyors in a systematic way. Finally, a survey of State Medicaid reimbursement and quality assurance officials is being designed to identify which States may hold the greatest potential for the use of Medicaid data in the survey process.

The Development of Long Term Care Reform Strategy for New York's Office of Mental Retardation and Developmental Disabilities

Period: June 1988-June 1990
TotalFunding: $115,581
Awardee: New York State Department of Social Services
Division of Medical Assistance
40 North Pearl Street
Albany, New York 12243
Investigator: Howard Gold

The New York Office of Mental Retardation and Developmental Disabilities will conduct a 2-year project to develop a comprehensive plan and waiver application that would reform the financing, regulation, and service delivery of the Mental Retardation (MR)/Developmental Disabilities system in three districts that cover eight New York counties. The State sees the demonstration as the first step toward statewide implementation. The objectives are to: 1) develop a financing system that will improve services to this population by expanding the number and types of people to be served and the types of services to be provided; 2) change the manner in which quality of care is assured; and 3) constrain growth in Federal expenditures for these services. Waivers would alter the Medicaid basis of payment, revise the State Medicaid plan requirements, change how Medicaid funds can be used, and implement revised quality assurance regulations. The demonstration will test an alternative financing approach that approximates recently formulated departmental policy directions as developed by the Department of Health and Human Services Working Groups on ICFs/MR. The project would represent a major test of reform in the delivery of services for persons who are developmentally disabled.

Both National and State level advisory panels have been convened, and the development of issue papers is underway.

The Multi-State Nursing Home Case-Mix and Quality Demonstration

Period: June 1989 - June 1993
Funding: $1,000,000
Awardee: State Medicaid Agencies in Kansas,
Maine, Mississippi, and South Dakota

This project builds upon past and current initiatives with case-mix payment and quality assurance. It will be a 4-year demonstration to design, implement, and evaluate a combined Medicare and Medicaid system in five States. The purpose of the demonstration is to test a resident information system with variables for classifying residents into homogeneous RUGS for equitable payment and for quality monitoring of outcomes adjusted for case mix. The new minimum data set for resident assessment will be used for both payment classification and quality monitoring systems. This information will be computerized, audited, and submitted as part of the billing documentation. It will be used to develop case mix adjusted outcome and process norms across the demonstration States. This system also will be used to trigger early quality reviews by State staff and provide the regular survey teams with information on potential problems in nursing facilities. It will have three phases: 1) systems development and design; 2) systems implementation and monitoring; and 3) evaluation. There will be 18 months of developmental work before the Medicare/Medicaid classification and payment system will be ready for implementation in the demonstration States.

The project has just started, the States have begun work on Phase I activities and will conduct their first data collection in spring 1990.

Long Term Care Case Mix and Quality Technical Design Project

Period:	September 15, 1989-September 14, 1991
Funding:	$997,887
Awardee:	The Circle, Inc. 8201 Greensboro Drive, Suite 600 McLean, Virginia 22102
Investigator:	Bob Burke, Ph.D.

This 2-year contract will support the design and early implementation phase of the Multi-State Nursing Home Case-Mix and Quality Demonstration. The first step will be to refine the data collection process creating consistent, reliable, and valid measurement of resident characteristics and staff time use across the four demonstration States (Kansas, Maine, Mississippi, and South Dakota). The demonstration will involve approximately 50,000 residents in 800 facilities at any one time. The second step will be to refine a resource utilization classification system that will apply to both Medicare and Medicaid residents in nursing facilities (SNFs and ICFs) across States. This system must be able to account for over 42 percent of the staff time variance in each of the several States. It must have natural breaks in the groups between residents who are expected to be short stayers vs. long stayers and between residents requiring

heavy technical nursing vs. residents with less technical needs. A prospective case-mix payment system to be used across the States for Medicare-covered stays will be developed using the common classification system. In addition, analyses comparing outcomes under different circumstances will be conducted. A national advisory group will be tasked to recommend the outcomes that are most promising for use in a quality monitoring system and to assist in the design of the quality monitoring system to be used during the operation phase of the demonstration.

New York State Integrated Quality Assurance System for Residential Health Care Facilities: The Next Step After Case-Mix Reimbursement

Period: August 1986-October 1990
Total Funding: $ 597,695
Awardee: New York State Department of Social Services
40 North Pearl Street
Albany, New York 12243
Investigator: Don Schnieder, Ph.D.

The objectives of the New York State Quality Assurance System (NYQAS) are to link data from the case-mix reimbursement system for use in the quality assurance system and to integrate the quality assurance processes of survey/certification, inspection of care, and utilization review. The State recently implemented a case-mix payment system for residential health care facilities for which all patients are assessed at least biannually. The resulting data on patient characteristics are audited and entered on a client-specific data base that can be utilized to target quality assurance activities toward facilities that:

- Have staffing patterns that seem inappropriate to needs of patients.
- Have excessive numbers of patients with clinical outcomes that indicate possible deficiencies in the quality of care.
- Have unexpected negative outcomes from one review to the next.

External outcome standards, survey and certification, inspection of care, and utilization review activities will be integrated into a single, patient-centered process. The use of the case-mix data base will serve to focus reviewer energies on problem facilities. The ability to routinely track significant or

potentially significant deteriorations in patient care will trigger off-cycle surveys. Facilities identified as having few or no problems will be targeted for abbreviated surveys.

The State has completed the NYQAS design has designed a training program for State surveyors on the use of the new protocols and procedures. The training began October 1988 and NYQAS was implemented in November 1988. Administrative waivers permit sampling of resident review (as opposed to 100 percent review), a survey cycle that averages 12 months (as opposed to 12 months for all homes), and the alignment of utilization review with case-mix assessment intervals.

FUTURE DIRECTIONS FOR LONG TERM CARE

During 1989, HCFA devoted substantial staff resources on the further development of demonstrations to test the cost-effectiveness of prospective payment systems for nursing homes and the development of quality measures to improve the quality of care in nursing homes and HHAs.

We will continue to test alternative financing schemes for long term care services, including patient-related or case-mix based prospective payment for SNF and ICF levels of care. Implementation of a demonstration of prospective payment methods for Medicare home health services will take place in 1990. We also intend to test the effectiveness of innovative State, local, and private programs to promote home care by the family or by other community support arrangements, such as in-home or other support services (adult day care, adult foster care, or shared housing), which substitute for or deter the use of institutional care for persons in need of long term care services. These efforts will include implementation of a large-scale demonstration directed at victims of Alzheimer's disease and related disorders. At the same time, we will continue to develop and test new approaches to more accurately "target" home health and community-based care in order to identify groups for whom reconfiguration of current service models can be cost-effective.

We also will develop and test outcomes of quality for nursing home and home health services and the applicability of using payment generated data to monitor quality. In this light, we will continue to develop a multi-State demonstration integrating patient assessment for a case-mix PPS for nursing homes with the quality assurance process for these providers.

Another very important area that will continue to be explored is alternative financing mechanisms for long term care. Although

the majority of the elderly are covered by both Medicare and supplemental insurance, a large portion of long term care services remain uncovered. Medicaid covers long term nursing care, but only after the elderly individuals have depleted their resources. Research is continuing that will identify the sources of financing for long term care at various points throughout institutionalization. This research will further examine characteristics of individuals who come to rely upon Medicaid for payment for their care. By identifying the risks associated with nursing home use, we hope to be able to propose improved methods of paying for this care. One alternative being studied as a solution for some of the elderly's problems in financing long term care is life care centers. Other ORD financing research continues to examine various States' reimbursement of long term care in order to assess the feasibility of recommending policy changes, e.g., prospective payment for SNF care.

Essential to the development of future long term care policies is the support for data collection and data analyses from projects that gather detailed information from representative national samples or other large segments of the elderly population. Research is continuing on the estimated future acute and long term care utilization based on information from available surveys on the morbidity, disability, and mortality of different birth cohorts. Data from the 1982 and 1984 Long Term Care surveys are being analyzed and plans continue for the 1989 survey. Data on the Medicaid program continue to be available on a person-level basis for some States from the Tape-to-Tape project.

OFFICE OF HUMAN DEVELOPMENT SERVICES

Administration on Aging

Long Term Care

AoA continued its support of long term care under Title IV-B of the Older Americans Act in 1989. The purpose of AoA's long term care activities is to develop a continuum of care ranging from prevention to maintaining maximum independence and self-sufficiency. AoA's long term care initiatives stem from a concern that chronically ill and functionally impaired older persons have access to appropriate community-based care in order to prevent premature or unnecessary institutionalization.

In FY 1989 AoA awarded 11 second year cooperative agreement awards to National Aging Resource Centers. Each Center is national in scope.

Six (6) of these Centers are pursuing the issue of the development of comprehensive, community based systems of long term care for older persons. Within the broad area of community based, long term care system development, each of these six (6) Centers focuses on one or more specific topical areas. The National Aging Resource Centers on Long Term Care are: Brandeis University, Bigel Institute for Health Policy, Waltham, MA; National Center for Senior Living, Heartland Center for Aging, South Bend, IN; University of California, Division of Geriatric Medicine, Los Angeles, CA; University of Minnesota, School of Public Health, Minneapolis, MN; University of South Florida, Suncoast Gerontology Center, Tampa, FL and National Association of State Units on Aging, Washington, DC. In addition, AoA has funded the National Association of State Units on Aging to establish the National Long Term Care Ombudsman Resource Center.

Four (4) additional National Aging Resource Centers address other related, topical areas of vital concern in the continued development of comprehensive, responsive systems of services to meet the needs (including long term care needs) of older persons and their families.

In addition, AoA is considering FY 1990 support for grants to States to assist them in planning the development of long term care systems. Such projects would emphasize coordination among key agencies and Governor's offices in such planning.

Funding for long term care efforts are as follows:

FY 1987	.2 million
FY 1988	1.6 million
FY 1989	2.9 million
FY 1990	2.9 million*
FY 1991	$ 2.9 million*

* Level of funding dependent upon second and third year continuation costs.

MENTAL RETARDATION
Obligations

	1987	1988	1989	Estimate 1990	Estimate 1991
Public Health Service:					
National Institutes of Health:					
National Institute of Child Health and Human Development	$46,221,000	$49,293,000	$48,257,000	$50,182,000	$52,221,000
National Institute of Neurological Disorders and Stroke	9,113,000	11,132,000	11,662,000	12,034,000	12,588,000
National Institute of Allergy and Infectious Diseases	13,371,000	13,373,000	14,903,000	15,207,000	16,057,000
Division of Research Resources	---	476,000	541,000	522,000	500,000
National Center for Nursing Research	21,000	18,000	25,000	25,000	25,000
Total, NIH	68,726,000	74,292,000	75,388,000	77,970,000	81,391,000
Health Resources and Services Administration: 1/	---	1,817,000	1,883,000	1,932,000	----
Centers for Disease Control:					
Immunization Program	87,361,000	98,198,000	126,800,000	156,183,000	152,722,000
Lead-Based Paint Poisoning Prevention Program	533,000	533,000	533,000	4,425,000	4,425,000
Total, CDC	87,894,000	98,731,000	127,333,000	160,608,000	157,147,000
Total, PHS	156,620,000	174,840,000	204,604,000	240,510,000	238,538,000
Social Security Administration:					
Estimated payments, benefits from OASDI trust funds	1,460,000,000	1,500,000,000	1,580,000,000	1,712,000,000	1,844,000,000
Estimated general fund payments for supplemental security income (Gross) 2/	1,402,000,000	1,621,000,000	2,282,000,000	2,264,000,000	2,632,000,000
Total, SSA	2,862,000,000	3,121,000,000	3,862,000,000	3,976,000,000	4,476,000,000
Health Care Financing Administration:	3,166,000,000	3,804,000,000	3,895,000,000	4,391,000,000	4,845,000,000
Total, DHHS	6,184,620,000	7,099,840,000	7,961,604,000	8,607,510,000	9,559,538,000

1/ Bureau of Maternal and Child Health and Resources Devlopment funds are not included due to the consolidated Maternal and Child Health Block Grant.

2/ Due to federal legislation mandating check payments on a banking day, the SSI program made 13 monthly payments in FY 1988, 11 monthly payments in FY 1990, and 12 monthly payments in other fiscal years.

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

MENTAL RETARDATION

At least six million people in the United States today are diagnosed with mental retardation. Although biomedical and behavioral scientists have sought and found the causes of approximately 350 types of mental retardation, more than three-quarters of all cases are unexplained. Researchers are working to solve these and other mysteries associated with mental retardation.

In simple terms, mental retardation is below average intellectual and social functioning manifested during the developmental years. Some biomedical causes can be diagnosed a few weeks after conception. However, when the cause is learning deprivation due to lack of stimulation during early childhood, the condition often is not detected until the child enters school. An IQ of 70 or below is generally considered an indication of mental retardation.

Children who are retarded because of impoverished environments are usually not severely retarded, but the impact on their lives and on society is tremendous.

Mental retardation that has physical origins can be caused by such diverse factors as a defective chromosome; a chemical imbalance; lead poisoning; birth trauma; certain bacterial, parasitic, and viral infections; brain injury, and maternal or infant malnutrition.

Because of the wide spectrum of disciplines spanned by research on this condition, research aimed at early detection, remediation, and, when possible, prevention of mental retardation is supported by several of the institutes of the National Institutes of Health, including the National Institute of Neurological Disorders and Stroke, the National Institute of Allergy and Infectious Diseases, the National Center for Nursing Research, and the Division of Research Resources. Primary responsibility for developing and supporting research in this field, however, rests with the National Institute of Child Health and Human Development (NICHD). Research in all institutes covers both biomedical and behavioral sciences.

Genetic Research

In genetics, this is a great age of discovery. Like Columbus--not realizing he had discovered America--the

implications in genetic research are not always immediately apparent.

In charting the myriad pathways of genetic messages that give us life, as well as illness and death, one scientist may find a defective chromosome that determines and transmits a rare disorder affecting a very small number of individuals. But that same investigator, or another, building on the knowledge gained, and conducting further research, may find that the same genetic defect is also a key to understanding more common disorders.

As a result of revolutionary breakthroughs in genetic research, treatment for human genetic diseases is now being developed in animal models.

Two major technical advances have made possible research that may one day lead to gene therapy of human disease:

1. The ability to duplicate (clone) a gene.

2. The development of viral carriers (vectors) that transfer such genes into many kinds of mammalian cells.

It is hoped that some genetic disorders can be treated by introducing a retrovirus carrying the missing gene into a person's own bone marrow. Retroviruses infect cells by directing them to copy and incorporate viral genetic instructions into the host cell's own DNA. The retrovirus would repopulate the entire bone marrow and give rise to new and healthy blood cells.

Grantees Dr. Jon A. Wolff of the University of Wisconsin at Madison, and Dr. Theodore Friedmann of the University of California School of Medicine, San Diego, have done major research in this new field, especially in disorders of purine metabolism, the cause of a number of severe and usually fatal illnesses which can cause retardation and for which there is no known cure.

Dr. Wolff's research into possible treatment or correction of inborn errors of metabolism, a frequent cause of mental retardation, has demonstrated that a virus carrying a genetic message into rat brains can alter certain biological abnormalities similar to those seen in Alzheimer's disease.

Dr. Wolff, with other researchers, is developing genetically modified cells that will be introduced into the genetic rat model of Parkinson's disease. This study explores the possibility of restoring nerve growth factor in the central nervous system.

These research projects have great relevance to genetically caused mental retardation and other inborn metabolic defects, since studies have shown genetic similarities between these developmental disorders and degenerative disorders, such as Alzheimer's and Parkinson's disease.

A project of major importance being conducted by NICHD grantees in Israel is exploring the cloning of genes on chromosome 21. When these genes are present in triplicate, they cause Down syndrome, the most common form of mental retardation associated with a genetic defect.

The researchers, headed by Dr. Yoram Groner of Weizmann Institute of Science, Rehovot, Israel, have succeeded in cloning two chromosome 21 genes. By injecting an extra one of these genes into fertilized mouse eggs, they have produced transgenic mice that have neurological, chemical, and physiological disorders characteristic of Down syndrome.

Researchers at The Johns Hopkins University School of Medicine in Baltimore, Maryland, headed by grantee Dr. Stylianos E. Antonarakis, recently reported cloning about one-fifth of human chromosome 21. They used a newly developed cloning technique that permits the duplication of much longer segments of DNA than was previously possible. The ability to copy chromosome 21 and to produce large quantities of isolated chromosomes will help researchers discover how its genes cause Down syndrome as well as an inherited form of Alzheimer's disease and other disorders.

Other Genetic Disorders

A genetic disorder called the Lowe Oculocerebrorenal syndrome (OCRL) results in mental retardation, cataracts, and defective kidney function. Grantee Dr. Dorothy Silver Reilly, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, is leading a team studying OCRL, with emphasis on using genetic probes to detect its carriers.

The chromosomal abnormalities peculiar to OCRL have been located in six families. Dr. Reilly's research has determined that genetic linkage analysis of family members can be an accurate method to determine OCRL carriers, when compared to findings of an ophthalmologic examination, the standard method of identifying carriers.

The syndrome called Cri Du Chat (cry of the cat) is characterized by severe mental retardation, microcephaly (small head), and other symptoms, most notable a high-pitched cry at birth which resembles the mewing of a cat. The syndrome occurs in approximately one in 45,000 live births,

making it a relatively common genetic disorder. Among institutionalized people with IQs below 50, the frequency of Cri Du Chat is estimated to be as high as one in 350.

Cytogenetic studies show that individuals with this syndrome have one normal and one partially deleted chromosome 5. In family studies, researchers have found that in 10 to 15 percent of the cases, there is a parental chromosomal rearrangement, usually involving the same incomplete chromosome 5. In the majority of cases the origin cannot be traced.

Grantees Drs. Leon R. Carlock and John J. Wasmuth at the University of California, Irvine, are analyzing this genetic defect at the molecular level. They have identified the first DNA fragments localized in the region of the damaged chromosome 5. The use of genetic and recombinant DNA techniques to study Cri Du Chat and other human deletion syndromes may lead to the understanding of how--and where--damaged genetic material produces some forms of mental retardation.

The peroxisome is a specialized organelle present in cells that synthesizes various acids and other chemicals in the body. Its importance has been overlooked until rather recently when scientists involved in gene mapping discovered that its absence or malfunction results in severe abnormalities, neurological defects, and usually very early death.

Dr. Hugo W. Moser, an NICHD grantee at the Kennedy Institute for Handicapped Children and The Johns Hopkins University, Baltimore, Maryland, is attempting to classify and trace the origins of peroxisomal disorders and to define the role of peroxisomes in normal development of the mammalian nervous system.

A characteristic of peroxisomal disorders is an excess of very long chain fatty acids, which accumulate in the tissues and cause such disorders as childhood adrenoleukodystrophy. This genetic disorder can strike apparently normal children at age three or four, gradually affecting their behavior, speech, and walking until they become spastic, unable to walk or swallow. Within a few years, they die.

Dr. Moser has traced the origin of the disorder to the terminal segment of the long arm of the X-chromosome. A DNA probe of this portion of the X-chromosome helps to detect carriers. Dr. Moser is carrying his investigations into the field of therapy. Together with Dr. William Rizzo, he is testing a diet that is restricted in very long chain fatty acids, combined with doses of glycerol trioleate and glycerol trierucate oil, which reduces, and in some cases, normalizes

the plasma level of long chain fatty acids. Preliminary clinical observations indicate that this course of treatment improves peripheral nerve function. Of great interest is a planned trial to test whether this regimen can prevent the onset of neurological disability in children who have this biochemical defect but have not yet developed symptoms.

Bio-Behavioral Research

Prematurity and low birth weight are major factors in neonatal death and a contributing factor in mental retardation of some infants who survive. NICHD is supporting several research projects that are searching for methods to identify as early as possible those infants at risk for mental retardation. This is important because the earlier remedial programs are started, the more potentially effective they are.

NICHD contractors Dr. Howard Golab, Dr. Barry Lester and colleagues at Pediatric Diagnostic Services, Inc., Cambridge, Massachusetts, are attempting to identify at-risk newborns by analyzing their cries. Measures of the most important acoustic characteristics of the cries of infants born after 40 weeks of gestation are fed into a computerized cry analysis system. At 18 months of age, these same infants are tested with standardized infant developmental scales. And at age five, they are given intelligence tests.

Preliminary results from a sample of children tested at these ages indicate that it is possible to use newborn cry characteristics to improve predictions about which infants will score low on later tests, compared with predictions based only on medical and socioeconomic status at birth.

Nutrition Research

Because it has been shown that nutrition strongly influences not only the general health of children but also their learning ability, NICHD is supporting many nutrition studies in the United States, Latin America and other countries.

Grantees under the direction of Dr. Reynaldo Martorell of Stanford University in California are now testing Guatemalan children who were born between 1970 and 1977 to assess the effects of nutritional supplements. In this longitudinal study, the diet of pregnant women and their infants was supplemented with extra protein. The effect of the supplemented diet on the children's social skills and intellectual achievements at age 10 to 18 is being evaluated.

In collaboration with researchers in Costa Rica, Dr. Betsy Lozoff of Case Western Reserve University, Cleveland, Ohio, is studying the neuro-behavioral effects of iron deficiency in infancy. Babies with iron deficiency anemia have lower mental and motor scores than non-anemic infants from similar environments. After three months of therapy, the children whose iron deficiency had been completely corrected no longer showed lowered mental and motor test scores. These children will be reevaluated at age 5.

In a similar multidisciplinary project in Bogota, Colombia, headed by grantee Dr. M. Guillermo Herrara of Harvard University, Cambridge, Massachusetts, mothers-to-be and infants were given dietary supplements, obstetric and pediatric health care, plus training to increase the psychological stimulation of their children. Not all of the mothers and children received all of these services because of the need to have a control group for comparison.

The children were followed until age 7. Results showed that those whose diets were supplemented through age 3 scored higher on growth and behavioral tests than children who did not receive supplements.

Home stimulation alone improved test scores on the speech and language subscales only. Nutritional supplementation, home stimulation, or a combination of both early in life, resulted in earlier school entry and greater likelihood that these children would pass from first to second grade. Maternal training also contributed to a better chance of an improved diet for the children, up to three years after supplements were no longer supplied. The children were then 7 years old, the age limit of the study.

NICHD is supporting two projects in India related to the mother's health during pregnancy and its effect on infant outcome. Both projects are under the direction of Dr. David Rush of Albert Einstein School of Medicine in New York City.

One project is investigating the relationship between maternal malnutrition and the outcome of pregnancy. This prospective study, which covers a large population at selected sites, began with a census of women. All those of reproductive age were weighed. These women will be followed periodically for regularity of menses in order to date pregnancy accurately and diagnose it early. Researchers will weigh the women, measure skinfold thickness and check their general health regularly. After the women give birth, their infants' health will be assessed and followed through one year of age.

The second project, being conducted at four sites in India, will try to determine the incidence of genital tract infection during pregnancy. The organisms that cause these

infections may be a contributing factor in the incidence of low birth weight and its many possible consequences, including mental retardation. Women identified as having such infections will be treated with antibiotics and the outcomes of their pregnancies will be assessed.

Lead Poisoning

Because children at highest risk for lead poisoning are generally from impoverished neighborhoods--where old, lead-based paint is peeling from various surfaces--it is difficult to separate out the problems caused by lead alone from those brought on by the effects of poverty and deprivation. It may be difficult to determine whether a school-age child is listless and inattentive because of exposure to lead or because of inadequate diet, lack of restful sleep, frequent infections, intellectual deprivation, or other consequences of poverty.

A major longitudinal study conducted by grantee Dr. Alan Leviton and the Mental Retardation Research Center at Children's Hospital, Boston, Massachusetts, has examined 1,512 children of parents whose socio-economic-educational levels put them at low risk for the lead poisoning often found in high-risk impoverished environments.

If a significant number of these children were found to have elevated blood lead levels combined with poor school performance, the cause of the poor school performance is more apt to be lead-related than if the children were subject to the multiple problems of deprivation.

In order to measure lead exposure in these children, Dr. Leviton used the shed baby teeth over an eight-year period in the life of each child. Teeth are good indicators of how much lead the child has absorbed, and they are readily available.

The full set of data on each subject included umbilical cord blood lead level, an interview with the mother at time of delivery, a questionnaire completed by each parent when the child reached age 7, the lead content of a deciduous tooth, and a questionnaire completed by the child's teacher when the child was age eight.

This study indicates that elevated lead levels in the teeth are associated with poor school performance and can impair other mental and behavioral functions.

Twice as many girls whose tooth lead level was 5 ppm or more tended to be withdrawn, self-destructive, inattentive, nervous/overactive, aggressive, or depressed than those with lower tooth lead levels.

Effects in boys with elevated lead levels were especially notable when their capacity to function was compared to that of their peers. Both boys and girls with higher than normal tooth lead levels were more easily distracted, more impulsive, had more difficulty following simple directions, had more problems concentrating and had more difficulty reading than those with low tooth lead levels.

Another finding of this study was that tooth lead measurements are more accurate indicators of the effect of lead levels in the body than are umbilical cord blood levels, and effects appear to be more apparent in girls than in boys.

Down Syndrome

To the general public, Down syndrome is synonymous with mental retardation. But there is now strong evidence that stimulation as infants with consistent follow-up enrichment can lift some of these children into more normal functioning.

Grantee Dr. K.E. Wisniewski of the New York State Office of Mental Retardation and Developmental Disabilities, Staten Island, New York, is doing research that suggests that children with Down syndrome may have previously unrecognized abilities and that some of the disabilities among these children may be due to causes other than Down syndrome.

A total of 239 persons with Down syndrome ranging from age 2 to 67 were given neurological and psychological tests. Eleven children and six adults were found to be not retarded, despite their diagnosis of Down syndrome. These seventeen had received early childhood stimulation and/or participated in academic mainstreaming.

All of the children in the study who were under age 10, and some in their teens, had begun attending infant stimulation programs as early as one to two weeks of age. In addition, they had been raised at home by parents actively involved in their education.

In general, the younger persons with Down syndrome functioned on a higher level than did the older ones, a fact presumably due to early and continued enrichment, including academic mainstreaming.

Only 16 of the individuals with Down syndrome under age 20 had severe mental retardation. In all cases, the mental retardation was intensified by factors other than the faulty chromosome associated with Down syndrome. For example, clinical records often revealed recurrent otitis media with transient or permanent hearing impairment.

All of those in their 50's or 60's tested in the mental retardation range. And 40 of the 61 persons over 30 years of age had severe or profound mental retardation. Most of these had been institutionalized as children.

Behavioral Research

Bar codes similar to those used in commercial packaging are helping slow readers, children with mental retardation, and sight-impaired individuals to learn reading skills.

SBI grantee Dr. Alan VanBiervliet of Learning Express, Inc., Little Rock, Arkansas, working with students in the Pulaski County School District of Arkansas and the Arizona School for the Deaf and Blind at Tucson, is applying bar code technology in the classroom.

The system involves passing a light-sensitive pen or laser over a printed code of bars that correspond to coded numbers. In retail stores, information on bar-coded products is stored in electronic memory, which can be accessed and presented visually or spoken with the aid of a voice synthesizer. This same technology is used in the Magic Wand Speaking Reader, a low-cost, durable, easily programmed computer developed by Texas Instruments as an educational toy to read, decode and use learning programs in bar-coded form called "Talking Tracks." Coded instructions produce words (spoken and/or printed), sentences, sound effects, music and a variety of instructions.

Children with learning problems, as well as sight-impaired children in the study, generally learn the system quickly and enjoy it. Once they learn to do it on their own, their reading scores improve dramatically.

The Magic Wand Speaking Reader is especially effective when handicapped children are mainstreamed. The system allows them to advance at their own pace, gives them self-motivation, and pleasure in the learning process.

Much of the literature on mental retardation in the 1960s and 1970s suggests that after the age of 14 many mildly mentally retarded individuals disappeared from mental retardation services and were apparently living as self-supporting, socially competent members of society ..... indistinguishable from the rest of the community.

Drs. Stephen A. Richardson, Helene Koller, and Mindy Katz of the Albert Einstein College of Medicine, The Bronx, New York, questioned those conclusions.

They focused on a group of 154 males and females with mild mental retardation, born between 1951 through 1955, who

were living in Aberdeen, Scotland in 1962. They were matched with a non-retarded sample of the same age. Both were traced from childhood to age 22 years, 3 months.

Results were less assuring than the earlier assumptions.

This new research showed that of all the subjects with mild mental retardation who had received supportive/ rehabilitative services as adults, 50 percent of the males and 60 percent of the females never held jobs in open employment.

Among those employed at age 22, 63 percent of the males who had no adult services held unskilled jobs. Of the non-retarded comparison subjects, 24 percent were in unskilled jobs. Because of a large number of variables--length of employment, skilled vs. unskilled work, promotions, etc.--it was impossible to do across-the-board comparisons between the job histories of retarded and non-retarded workers, males and females.

Some facts were apparent, however. Those with mental retardation did not progress into skilled jobs, as did the comparison subjects. They received significantly less pay than did the non-retarded because salaries are generally related to job skills. And those who had no services especially felt that illiteracy and lack of math skills held them back.

In a follow-up study focused on the worker's viewpoint, done by the same researchers, results indicated that mildly retarded workers disliked boring and tedious, repetitive jobs just as much as non-retarded individuals. Of all reasons for leaving a job, "not enough pay" was cited most frequently, and more often by males than by females.

Enrichment Programs

Among the most promising research efforts supported by the NICHD are those showing the dramatic outcomes of early childhood enrichment programs on children from impoverished homes. Most of these children are deprived of intellectual stimulation in the developmental years. Many are also undernourished or malnourished. A large number are children of retarded mothers.

They form a large component of the population with mental retardation. And it has been shown that this type of functional retardation can be prevented by early intervention.

One of the ongoing, major studies that has received long-term support from the NICHD is being conducted under

grant support at the Mental Retardation Center at Chapel Hill, North Carolina. Dr. Craig Ramey, the principal investigator, has shown that children of retarded mothers who received educational interventions throughout the first five years of life were nearly six times more likely to function within the normal range than those who had not been helped.

The intervention has had broad effects on the family as well. For example, teenage mothers of children in the program were apt to complete high school and later continue with post-high school education, to receive less or no welfare, and to have smaller families than comparable mothers of children in the control group.

National Institute of Neurological Disorders and Stroke

The National Institute of Neurological Disorders and Stroke (NINDS) is the national focal point for biomedical research on conditions that can contribute to mental retardation by damaging the central nervous system early in life.

Treating Amino Acid Disorders

Disorders of the metabolism of amino acids, molecules vital for normal growth, can result in mental retardation and delayed motor development. But two recent studies funded by the NINDS show that certain amino acid disorders can be treated successfully, if they are treated early.

Dr. Vivian Shih at the Massachusetts General Hospital in Boston has treated children with hyperphenylalaninemia, an amino acid disorder, using folinic acid. In a small group of patients, treatment in the first year of life prevented delayed mental and motor development normally associated with this disorder. The treatment also reduced the severity of neurological damage in early childhood. In addition, a separate trial by Dr. Shih confirmed the importance of early dietary therapy in preventing neurological damage in children born to mothers with phenylketonuria, an inability to metabolize phenylalanine. She found that diet therapy (to limit phenylalanine) begun before conception or in the first three months of pregnancy resulted in normal offspring. However, poor dietary compliance or diet therapy not begun until the sixth month of pregnancy resulted in small brain size and delayed motor development.

Understanding Autism

More than 5 of every 10,000 babies are born with autism, a developmental disorder of the brain. As they age, these children experience slow development of language, cognition, and social behavior. Approximately 60 percent of these children are severely mentally retarded.

Many autistic children also have abnormal postural control, which expresses itself in unusual ways of holding the body. Thus far, there has been little systematic measurement of this symptom. But recent research by NINDS grantee Dr. Reuben Kohen-Raz of the Hebrew University of Jerusalem has shown that autistic children have abnormal rigidity and jerkiness in the legs and feet and an unusual preference for balancing their weight on a single foot, toe, or heel during normal standing. Because these abnormalities may be caused by specific structural defects in the brain,

findings like those of Dr. Kohen-Raz could aid efforts to locate the site of neuroanatomical damage in autistic children.

The cause of autism is unknown. As a result, scientists are searching for biological abnormalities that may yield clues about the origins of this disorder. For example, NINDS grantee Dr. Isabelle Rapin of Albert Einstein College of Medicine in the Bronx, New York, is studying electrical activity of the brain in autistic patients. Dr. Rapin's research will look for a link between abnormal brain activity and the deviant cognitive and emotional development that is specific to autism.

National Institute of Allergy and Infectious Diseases

Diseases and infections passed from mother to child, either before or during birth, can cause serious health problems in the newborn, including mental retardation. The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports research aimed at the prevention and control of infections and diseases that can cause mental retardation.

Bacterial meningitis causes an estimated 5 to 15 percent of cases of mental retardation. Meningitis is an inflammation of the membranes that cover the brain and spinal cord. Even with treatment, meningitis can be fatal. Because the disease can progress so quickly and because there is still no vaccine effective in infants, it is of the utmost importance that improved methods of prevention and treatment be found.

Group B Streptococcal Infections

Group B streptococcus (GBS) is a bacterium that can infect pregnant women and be passed to a baby in the birth canal during delivery. GBS causes life-threatening infections, including meningitis, in nearly 11,000 babies a year. Approximately 55 percent of premature babies and 15 percent of full-term babies who have GBS infection die each year.

Researchers have long thought that immunizing pregnant women against GBS infections would also protect the fetus. NIAID grantee Dr. Carol Baker at Baylor College of Medicine in Houston, Texas, and her colleagues have developed a vaccine that, when given to pregnant mothers, shows promise in protecting the fetus from GBS infection.

In the study, 40 pregnant women were vaccinated with a single dose of a carbohydrate component of GBS. A mild tenderness at the site of the injection in nine women was the only adverse effect. The fetuses experienced no side effects. Sixty-three percent of the women responded to the vaccine. Of those, 80 percent of their infants were protected by antibodies to GBS at one month of age, and 64 percent were still protected at three months. (An antibody is a protein in the blood that protects the body from a foreign organism.) None of the babies developed symptomatic GBS infection.

Herpes Simplex Virus Infection

Transmission of herpes simplex virus (HSV) infection from mother to baby during delivery is another major cause of mental retardation in newborn infants. One way to help protect the newborn is to establish ways in which the mother can more easily recognize the signs of herpes virus infection.

NIAID grantee Dr. Lawrence Corey and his colleagues at the University of Washington School of Medicine in Seattle studied ninety-five women with HSV-1 or HSV-2 antibodies but no previously reported symptoms of genital herpes. These women were examined and tested periodically for evidence of active infection.

Dr. Corey found that approximately 50 percent of women infected with HSV type-2 who reported no symptoms of HSV-2 infection actually did experience symptoms that they did not recognize as being herpetic (caused by HSV-2). In addition to being examined and tested, the women attended counseling sessions, where typical herpetic lesions were described. They were informed about the association of genital herpes with breaks in the skin, mild external irritation or itching, or red blotches. Through the counseling session, the researchers illustrated that many persons with HSV-2 infection who initially report no symptoms can be effectively counseled and taught to recognize symptoms of genital HSV infections. This is important because women who have active HSV-2 infections at the time of delivery should have a Cesarean section so that the baby will not be infected by passage through the birth canal.

Outlook

Research tools employing biotechnology are continuing to make progress in understanding mental retardation at its molecular level. Someday, this increased understanding may permit mental retardation to be treated or prevented, possibly even before birth.

Until that time, research continues on developing approaches and techniques to ameliorate the effects of mental retardation in affected individuals. This is being made possible by unraveling the components of speech acquisition and other cognitive function so that appropriate intervention strategies can be designed.

HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Health Professions

Mental Health Activities

Thirty-two Physician Assistant Training programs offered 1,615 students exposure to mental health issues. Psychiatric clinical rotations included inpatient and out patient encounters, with an emphasis on mental health or psychosocial experiences commonly seen in primary care practice. Funds in the amount of $43,889 were specifically requested for activities in this area. These activities are consistent with the strong emphasis placed on behavioral sciences in Physician Assistant training and the importance placed on interpersonal and psychosocial skills.

Eighty-three residency programs under General Internal Medicine and General Pediatrics indicated a commitment to training in mental health care. An estimated 857 individuals will benefit from these programs. Sixty-seven of these programs received awards totaling $1,636,111. Under the faculty development grant program, two grantees indicated mental health activities that would effect the faculty training of 54 individuals.

Eleven Area Health Education Center programs indicated having mental health education activities and were awarded a total of $202,834 for these efforts, estimated to affect 220,235 individuals. The WAMI AHEC program received the largest award ($79,069) specifically for these activities.

Three Family Medicine Predoctoral Training program grantees indicated a commitment to mental health education. Residency training in Family Medicine will include mental health emphasis for an estimated 239 residents among 9 grantee programs. A total of $21,406 was awarded among these programs specifically for these activities.

Faculty training projects in Geriatric Medicine and Dentistry will include emphasis in the area of mental health for 67 fellows in 22 of the projects supported by the Bureau.

Mental health issues related to HIV/AIDS will be addressed in the training offered by 4 AIDS Regional Educational and Training Center grantees.

CENTERS FOR DISEASE CONTROL

Immunization
Mental Retardation

A rubella epidemic occurred in the United States in 1964-65 and resulted in an estimated 30,000 cases of congenital rubella syndrome (severe birth defects) and left nearly 15,000 babies mentally retarded, deaf, or blind. In 1970 when a rubella vaccine became available for use, the Centers for Disease Control provided project grants and technical assistance to State and local health agencies to support an intensive rubella immunization program. In 1970, 56,552 rubella cases were reported and 31 deaths occurred.

One of the program goals of the Immunization Initiative, which began in 1977, was to raise immunization levels of children under age 15 against rubella to at least 90 percent by October 1, 1979. This goal was exceeded by that date, and the rubella immunization level is presently 98 percent, as indicated by the review of school-enterers immunization records during the 1988-89 school year.

Reduction of disease morbidity is the ultimate goal. In 1989, 394 cases of rubella have been reported through the first 48 weeks. In 1988 a total of 225 rubella cases were reported. Only 6 cases of congenital rubella syndrome were reported in 1988 and 3 cases have been reported through the first 48 weeks of 1989.

Appropriate administration of safe and effective vaccines remains the most cost-effective method of preventing human suffering and reducing economic costs resulting from vaccine-preventable diseases. Since 1963, the Centers for Disease Control has provided project grant support to assist State and local health agencies in planning, developing, and conducting childhood immunization programs. The funding for FY 1989 was $126.8 million.

Benefit-cost analysis of immunizations demonstrates high rates of return and indicates that immunization programs make an important contribution to health sector cost containment efforts as well as to the quality of life of the communities served. For example, it is estimated that measles immunization currently saves approximately $500 million per year, and that polio immunization saves about $1 billion per year. Over 71 million cases of measles and 23,100 cases of mental retardation have been averted, and 7,100 children's lives have been saved because of measles immunization.

State and local immunization programs, supported by these funds and other Federal resources, have raised immunization levels higher than ever before, and reduced the reported occurrence of most vaccine-preventable diseases to the lowest levels ever, or to near record lows. The following data describe the latest immunization levels and reported disease incidence:

Disease	Immunization Levels (National Weighted Results) 1987-88 School Year	1988-89 School Year	Reported Cases 1988	1989#
Measles	98%	98%	3,396	14,226
Rubella	98%	98%	225**	394
Polio *	97%	97%	9	0
Diphtheria	97%	97%	2	3
Tetanus	97%	97%	53	41
Pertussis	97%	97%	3,450	3,392
Mumps	98%	98%	4,866	5,066

First 48 weeks of 1989.
*Subject to change due to retrospective case evaluations or late reporting
**Record low

With the attainment of these immunization levels, major epidemics of these diseases have been eliminated and the backlog of underimmunized school-age children has been virtually eliminated. In addition, grant resources support local disease surveillance and outbreak control activities, local assessment of immunization levels and coverage, local public awareness activities, and local laboratory services.

These State and local activities are complemented by activities performed at CDC which can either be accomplished better at the national level or which are more cost effective to perform centrally rather than being duplicated in each State and Territory. These activities include providing technical assistance and consultation in management practices and program operation methods; developing national goals for the prevention and control of childhood vaccine-preventable diseases and the strategies for achieving these goals; reviewing and evaluating State and local immunization programs; maintaining a stockpile of vaccine and jet injector equipment for use to control epidemics or in the event of disruption in vaccine supply; maintaining a mechanism for the saving of millions of dollars annually in the consolidated purchase of vaccines; providing national surveillance of vaccine-preventable diseases and prompt epidemic assistance in the investigation and control of outbreaks of diseases; providing laboratory reference services; rapidly identifying of problems of national significance (e.g., the identification of vaccine lots that are of potential concern regarding safety); developing recommendations for the appropriate use of vaccines; assessing national immunization levels; laboratory proficiency testing and quality control; and conducting studies and investigations to determine the safety, efficacy, and appropriate use of new and current vaccines.

The following 1989 accomplishments reflect the continuing progress being made as a result of multifaceted immunization programs involving a coordinated approach whereby Federal, State, and local governments have worked together toward a common goal:

a. Uniform case definitions of vaccine-preventable diseases developed by CDC have been implemented in all of the States.

b. There has been a decrease in reported measles during two of the past three years and indigenous measles has been reduced by approximately 99% compared to prevaccine years.

c. Approximately 68 percent of the 13,578 indigenous cases of measles reported during the first 48 weeks of 1989 were classified as non-preventable.

d. Eighty-three percent of the Nation's 3,138 counties have reported no measles cases during the first 48 weeks of 1989.

e. No cases of diphtheria and only two cases of tetanus were reported in children under age 15 in the first 48 weeks of 1989. Two cases of neonatal tetanus were reported.

f. Over twenty million doses of childhood vaccine were administered in the public sector.

g. Through November 1989 more than 1,395,000 doses of HbCV has been purchased using a combination of Federal, State and local funds.

h. Approximately 22 million doses (27 million doses if MMR is counted as 3 antigens) of vaccine were purchased through CDC vaccine contracts for use in State and local immunization programs.

i. All 50 States and the District of Columbia have immunization laws requiring immunization prior to the first entry into school. Forty-five of these areas now have Kindergarten through Grade 12 immunization requirements.

j. Fifty reporting areas have implemented hospital-based maternal immunization education programs which reach 90 percent of targeted hospitals.

k. Standard immunization record cards have been adopted in all 50 States and the District of Columbia.

l. Over 300,000 doses of influenza vaccine have been administered in 9 influenza vaccination demonstration projects.

The long-range goal of the immunization program is, through immunization, to eliminate indigenous measles, rubella, and congenital rubella syndrome from the U.S. and to reduce poliomyelitis (polio), mumps, diphtheria, pertussis and tetanus to levels so as not to be significant public health problems in the United States. Objectives for the Year 2000 are under development. The 1990 objectives are to assist in achieving the following:

- By 1990, reductions in the reported incidence rate of:

  1. Measles to fewer than 500 cases per year, all import-associated.

2. Mumps, rubella, and pertussis to fewer than 1,000 cases per year.

3. Diphtheria and tetanus to fewer than 50 cases per year.

4. Polio cases to fewer than 10 cases per year.

- By 1990, increases in the number of children immunized so that:

  1. Ninety percent of children will be immunized against measles, mumps, rubella, diphtheria, pertussis, and tetanus by the end of their second year of life.

  2. Ninety-five percent of children attending licensed day-care centers and kindergarten-grade 12 should be fully immunized.

- By 1990, refined and improved surveillance and evaluation systems so that:

  1. At least 95 percent of all children through age 18 have up-to-date official immunization records in a uniform format using common guidelines for completion of immunizations.

  2. At least 90 percent of those hospitalized and 50 percent of those not hospitalized with vaccine-preventable diseases are reported.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

SOCIAL SECURITY ADMINISTRATION

Mental Retardation

Purpose

The basic purpose of the social insurance programs (Old-Age, Survivors, and Disability) is to provide cash benefits to replace, in part, earnings that are lost to individuals and families when earnings stop or are reduced because the worker retires, dies, or becomes disabled. This program is contributory and self-supporting. Benefits are wage-related and entitlement to benefits is an earned right. In January 1974, the Supplemental Security Income program was added to those SSA administers. It provides payments to the needy aged, blind, and disabled, is noncontributory and is financed entirely out of general Federal revenues.

Historical Development

In 1935, when the original Social Security law was passed, the program was to have provided only retirement benefits to aged workers. In 1939, benefits for dependents and survivors were added and benefits became payable in 1940. Protection against long-term total disability--not only for disabled workers, but also for adult children (who became disabled before age 18) of disabled, retired, or deceased workers--was provided by the 1956 amendments. The 1967 amendments provided benefits for disabled widows and widowers age 50 and over. From 1939 through 1974, Congress granted ten general benefit increases in recognition of the fact that prices and wages had increased. In 1972, a section of P.L. 92-336 provided for an automatic benefit increase when the cost-of-living rises by 3 percent or more. The 3 percent minimum was eliminated in 1987. Effective January 1974, payments under the Supplemental Security Income program began to qualified aged, blind, and disabled persons, including the mentally retarded.

Economic Impact

Old-Age, Survivors and Disability Insurance (Title II Program)

Mental retardation is a major factor in about 70 percent of cases involving dependents or survivors who have been continually disabled since childhood. In fiscal year 1989 an estimated 543,000 mentally retarded adults disabled in childhood, and retarded workers received $1.6 billion in benefits.

Standards as to the level of severity required in disability cases involving mental retardation are published in regulations. These regulations have the effect of law and are available to the public and medical community.

The number of mentally retarded children under age 18 who receive Social Security insurance payments as dependents of retired, disabled, or deceased workers is unknown, since their benefits are payable regardless of disability. Under Social Security's "Childhood Disability" provisions, lifetime monthly payments can be made to a person age 18 or over who has been disabled by

mental retardation--or other impairments--since childhood. In many cases, the monthly benefits enable the retarded childhood disability beneficiary to be cared for at home instead of in an institution. Furthermore, as more and more retarded people outlive their parents, the program offers reassurance to fathers and mothers who know that financial help for their disabled child will be provided even after their deaths. About 60 percent of the childhood disability beneficiaries are age 35 and over and about 35 percent of them are age 45 and over.

If the parents are dead, a relative or other party who has demonstrated a continuing interest in the beneficiary's welfare, a welfare agency, or a legal guardian may be chosen as representative payee to handle the benefit funds and to plan their use on behalf of the beneficiary. Each representative payee is held accountable for the way in which the benefits are used.

Supplemental Security Income (Title XVI)

An estimated 512,000 retarded individuals who are not entitled to benefits under the title II Disability Insurance program were receiving payment under the Supplemental Security Income program in June 1989. (This figure includes those recipients receiving only a State supplementary payment).

Activities and Achievements

Since 1970, the Social Security Administration has conducted periodic onsite reviews in State mental hospitals and schools for the retarded. Currently SSA performs triennial reviews. The program focus is an indepth examination of the way in which these institutions are managing Social Security benefits on behalf of patients who receive their checks through an institutional official serving as "representative payee."

The observations and conclusions resulting from a State review are communicated to the State Commissioner for their use in the development of improved practices in the State's system. Findings also serve as a basis for SSA program and policy evaluation. The onsite approach is expected to strengthen relationships with the States, improve their understanding of their responsibility for optimum use of benefits when serving as representative payee, and open new channels for the discussion of problems and practices affecting the well-being of all beneficiary-patients in State mental institutions.

SSA has participated in the Special Program for Employment of the Handicapped since its inception in 1964 to employ the mentally retarded. It also has tried to generate interest in the program by private employers and other Federal agencies. In SSA, mentally retarded persons are successfully performing in such positions as mail and file clerks, messengers, operators of printing, xerox, card reader machines, and key punch machines. An experiment with the color coding of file cabinets and cartridges of microfilm has proven highly successful in broadening employment opportunities for the mentally retarded to an area of work which requires a very high degree of accuracy.

SOCIAL SECURITY ADMINISTRATION

Annual Payments to the Mentally Retarded
FY 1987 - FY 1991
(In Millions of Dollars)

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
Estimated Benefit Payments from OASDI Trust Funds	$1,460	$1,500	$1,580	$1,712	$1,844
Estimated General Fund Payments for Supplemental Security Income (Gross)	1,402	1,621	2,282	2,264 1/	2,632
Total, Social Security Administration	$2,862	$3,121	$3,862	$3,976	$4,476

1/ Due to Federal legislation mandating check payment on a banking day, the SSI program made 13 monthly payments in FY 1988, will make 11 monthly payments in FY 1990, and 12 monthly payments in other fiscal years.

HEALTH CARE FINANCING ADMINISTRATION

MENTAL RETARDATION

Effective January 1, 1972, P.L. 92-223 transferred intermediate care services to title XIX as an optional service and authorized the provision of intermediate care facility (ICF) services in public institutions for the mentally retarded if the institution provides health and rehabilitative services and if the eligible individuals are receiving active care and treatment. To assure that the Federal dollars made available for such institutional care could lead to higher quality care and services in an improved environment, and not simply to a replacement of State dollars, the legislation contained a provision requiring the States to maintain their own fiscal effort.

In FY 1990, 52 of the 57 Medicaid jurisdictions included, in their State plan, coverage of ICF services in public institutions for the mentally retarded; and 44 cover such services in private institutions. Prior to January 1, 1972, some 17 States claimed Federal matching for the mentally retarded in institutions which qualified as skilled nursing homes. It should be noted that because services in the past were being provided to the mentally retarded as skilled nursing home services, the adoption of the intermediate care facility program resulted in a redesignation of facilities in some States. The result is that these facilities are able to provide services at a more appropriate level of care where skilled nursing care is not medically necessary. States however, continue to provide care for the mentally retarded in skilled nursing facilities where medically appropriate. Also, Section 2176 of the omnibus Budget Reconciliation Act of 1981 allows States to provide care in the home by community-based services through an approved waiver process. As of December 1, 1989, there were 50 approved waivers to provide home and community-based services to the mentally retarded and developmentally disabled.

Total Federal expenditures for services for the institutionalized mentally retarded (in ICFs only) are estimated to be $4,845 million in FY 1991. Estimates are not available on the number of Medicaid dollars expended on all other Medicaid services provided to the mentally retarded. A Medicaid-eligible mentally retarded person may receive the full range of Medicaid services, and receive them on the same basis as the rest of the Medicaid eligible population.

ESTIMATED FEDERAL MEDICAID EXPENDITURES FOR INTERMEDIATE CARE FACILITIES / MENTALLY RETARDED
(dollars in millions)

FY 1989	FY 1990	FY 1991
$3,895	$4,391	$4,845

DEPARTMENT OF HEALTH AND HUMAN SERVICES

MIGRANT PROGRAMS

Funds Expended for Migrants
(amounts in thousands dollars)

PUBLIC HEALTH SERVICES:

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
Health Resources and Services Administration					
1. Bureau of Health Professions — Area Health Education Centers.....	$ 105	$ 235	$ 359	$ 384	—
2. Bureau of Health Care Delivery and Assistance.....	45,400	44,423	45,646	47,369	48,369
Subtotal	45,505	44,658	46,005	47,753	48,369
HUMAN DEVELOPMENT SERVICES:					
Administration for Children Youth and Families					
1. Head Start Program	40,674	44,345	45,419	52,095	63,637
Total, Migrant Programs	$85,179	$89,003	$91,424	$99,848	$112,006

HEALTH RESOURCES AND SERVICES ADMINISTRATION

Bureau of Health Professions

MIGRANT HEALTH

Six of the Bureau's grant programs reporting offering training experiences in migrant health during FY 1989. A total of $386,162 was awarded among the grantees specifically for these activities, which are estimated to impact 98,801 individuals.

The Area Health Education Center program provided significant support for migrant health through 7 of its projects which specifically reported these activities. These awards totaled $358,790 and 98,765 individuals were estimated to be impacted.

One General Internal Medicine/General Pediatrics Residency Training program requested $14,932 for its activities related to migrant health. Twelve residents will benefits from this training.

Only one of the Family Medicine training programs indicated activity specifically related to migrant health. The section 786(a) graduate training program supports migrant health training specifically at these institutions. The University of North Carolina Chapel Hill is developing a training site in a rural area to provide care to underserved and migrant populations.

Migrant health activities are part of 3 Physician Assistant training programs supported by the Bureau. Twenty-one students will benefits from this training for which a total of $12,440 was requested specifically by the grantees.

The Geriatric Medicine and Dentistry Faculty Training Projects program will include 3 faculty in migrant health training activities as reported by one training project.

Migrant health issues will be included in HIV/AIDS training at five of the AIDS Regional Education and Training Centers supported by the Division of Medicine.

HEALTH RESOURCES AND SERVICES ADMINISTRATION

Bureau of Health Care Delivery and Assistance

MIGRANT HEALTH

The purpose of the Migrant Health program is to assure access to and the provision o an adequate level of health care services for migrant and seasonal farmworkers and dependents. In Fiscal Year (FY) 1989, grants were made to public and private nonprofit organizations.

During this period the Migrant Health program supported 400 clinics. These centers provided the main source of health services to the Nation's 2,700,000 migrant and seasonal farmworkers and their families. During 1989, these centers provided services to approximately 500,000 persons.

Migrant health centers, either through their employed staff or through contracts with other public or private entities, provide health delivery services including services of physicians and, where feasible, services of physicians' assistants and nurse clinicians, diagnostic laboratory and radiology services, preventive health services, infant mortality activities authorized by P.L. 100-386, transportation, preventive dental services and pharmaceutical services. Case management approaches are used to ensure the delivery of these essential health care services that must be coordinated for a transient population. The program is continuing to conduct environmental health assessment activities including detection and alleviation of unhealthful conditions associated with water supply, sewage treatment, solid waste disposal, rodent and parasitic infestation, and field sanitation. The program also conducts accident prevention programs, programs to eliminate excessive pesticide exposure, and programs to improve housing.

In FY 1990, the program will continue services to 500,000 migrant and seasonal farmworkers and their families.

The FY 1991 request of $48,369,000 is an increase of $1,000,000 over the FY 1990 current estimate and would provide for continued health care services to approximately 500,000 migrant and seasonal farmworkers and their families.

HUMAN DEVELOPMENT SERVICES

Administration for Children, Youth and Families

MIGRANT HEAD START PROGRAM

The Indian and Migrant Program Division in the Administration for Children, Youth and Families funds grantees to provide comprehensive developmental services to migrant pre-school children and their families.

Because of the unique needs of migrant farmworking families, programs had to be designed to provide the family with access to these resources without creating economic or other hardships. Resources alone, without an adequate system of delivery, will not solve the problems of migrant families with pre-school children.

The children are served through a basic program design which incorporates Head Start standards and quality child care services. This design calls for some structural modifications of the traditional Head Start program including: (1) extending the hours of operation to coincide with the parent's working hours; (2) allowing all pre-school children to participate, including infants, and (3) utilizing bilingual and bicultural staff where needed. These modifications are necessary in order to provide the type of full service program which is tailored to the needs of migrant families.

Head Start funds for training and technical assistance projects provide direct assistance to Migrant Head Start programs. Other ACYF funds are used to support child abuse prevention and treatment activities in Head Start programs and experimental and research activities.

MINORITY HEALTH AND ASSISTANCE TO MINORITY HEALTH STUDENTS AND SCHOOLS
Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
National Institutes of Health:					
National Heart, Lung, and Blood Institute	$58,178,000	$58,836,000	$69,833,000	$79,786,000	$83,431,000
National Cancer Institute	27,154,000	28,454,000	35,649,000	39,599,000	41,758,000
National Institute of Dental Research	2,528,000	3,043,000	3,854,000	3,993,000	4,141,000
National Institute of Diabetes and Digestive and Kidney Diseases	23,075,000	24,612,000	28,404,000	29,200,000	34,000,000
National Institute of Neurological Disorders and Stroke	3,612,000	6,149,000	5,925,000	6,114,000	6,396,000
National Institute of Allergy and Infectious Diseases	7,336,000	17,240,000	22,401,000	28,806,000	39,000,000
National Institute of General Medical Sciences	46,148,000	47,005,000	46,863,000	50,292,000	56,404,000
National Institute of Child Health and Human Development	52,312,000	66,988,000	74,813,000	78,000,000	81,200,000
National Eye Institute	1,400,000	1,595,000	1,872,000	1,976,000	2,098,000
National Institute of Environmental Health Sciences	---	---	5,000,000	5,150,000	5,305,000
National Institute on Aging	2,895,000	3,678,000	4,016,000	4,946,000	5,113,000
National Institute of Arthritis and Musculoskeletal and Skin Diseases	13,845,000	12,289,000	12,471,000	13,839,000	14,529,000

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
National Institute of Deafness and Other Communication Disorders	---	---	224,000	1,061,000	1,101,000
Division of Research Resources	16,223,000	21,229,000	25,877,000	27,787,000	33,188,000
National Center for Nursing Research	529,000	1,132,000	2,195,000	2,700,000	2,700,000
Minority Access to Research Careers National Institute of General Medical Sciences (NIGMS)	(8,566,000)	(8,709,000)	(9,053,000)	(10,670,000)	(13,359,000)
Minority Biomedical Research Support, (NIGMS)	(37,582,000)	(38,296,000)	(37,810,000)	(39,622,000)	(43,045,000)
Research Centers in Minority Institutions Program (DRR)	(10,000,000)	(11,010,000)	(17,171,000)	(19,337,000)	(24,667,000)
TOTAL, NIH	255,235,000	292,250,000	339,397,000	373,249,000	410,364,000

MINORITY HEALTH AND ASSISTANCE

Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
Public Health Service:					
Alcohol, Drug Abuse, and Mental Health Administration 1/	$13,531,000	$15,984,000	$58,245,000	$88,930,000	$86,053,000
Health Resources and Services Administration	41,250,000	45,850,000	47,389,000	48,097,000	164,578,000
Center of Disease Control	55,386,000	61,560,000	87,427,000	125,766,000	129,351,000
Office of the Assistant Secretary for Health	2,950,000	2,793,000	2,949,000	3,946,000	14,962,000
Agency for Health Care Policy and Research	2,500,000	2,663,000	951,000	4,930,000	4,930,000
TOTAL, PHS.....	$370,852,000	$421,100,000	$536,358,000	$644,918,000	$810,238,000

1/ Excludes ADMHA's Block Grant

NATIONAL INSTITUTES OF HEALTH

Nat onal Heart, Lung, and Blood Institute

MINORITY HEALTH AND ASSISTANCE TO MINORITY STUDENTS AND SCHOOLS

Minority programs of the National Institutes of Health (NIH) are primarily in two areas: 1) minority health and 2) assistance to minority students and schools. Programs in minority health include research and education activities related to diseases having greater morbidity and mortality in minority populations, as well as research on cultural differences that may facilitate or impede the dissemination of health information or the delivery of health care to minorities. Programs to assist minority students and schools provide support for training and career development to encourage minority students and scientists to pursue biomedical research careers. Minority programs target four ethnic minority populations: blacks, Hispanics, Native Americans, and Asian/Pacific Islanders.

The National Heart, Lung, and Blood Institute (NHLBI) has a long history of support for minority programs focusing on both minority health and assistance to minority students and schools.

MINORITY HEALTH

One of the first major programs to investigate cardiovascular health in blacks began in 1957 and continues today. This study, the Evans County Study, was initiated by Dr. Curtis G. Hames of Claxton, Georgia, in collaboration with investigators at the University of North Carolina School of Public Health and with the encouragement and assistance of the Director of the then National Heart Institute, Dr. James Watt. Important data obtained during the past 30 years on black-white differences in risk factors for coronary heart disease (disease of the arteries supplying the heart) and hypertension (high blood pressure) are derived from this study.

Although most minority-related programs supported by the NHLBI focus on blacks, development of research related to Hispanic, Native American, and Asian/Pacific Islander populations is being encouraged. In the Diabetes and Cardiovascular Diseases Among Hispanics program, for example, all participants are Hispanic. A program on cardiovascular disease in American Indians began in fiscal year 1988. Among the Asian/Pacific Islander programs is one of the NHLBI's longest ongoing studies, the Honolulu Heart Program, which started in 1965. The program's goal is to collect epidemiologic and pathologic data on heart disease from a cohort of 8,004 men of Japanese ancestry living in Hawaii.

Morbidity and Mortality From Heart, Blood Vessel, Lung, and Blood Diseases

Heart and Blood Vessel Diseases -- The mortality and prevalence rates for coronary heart disease are similar in black and white males. However, black females have higher rates than do white females. Blacks have high prevalence rates for angina and higher case fatality rates for myocardial infarction than whites. Risk factor studies indicate that blacks in the United States are at

increased risk of coronary heart disease due to hypertension, diabetes mellitus, certain cardiac abnormalities such as left ventricular hypertrophy, and obesity (in black women).

Hypertension is a major risk factor for heart and blood vessel disease in black Americans. Mean blood pressure levels are higher in blacks than in whites and more blacks than whites have definite, borderline, and isolated systolic hypertension. Data from the National Health and Nutrition Examination Surveys (NHANES II, 1976-1980) indicate that the prevalence of definite hypertension in people 25 to 76 years of age was as follows: 28 percent in black males, 21 percent in white males, 30 percent in black females, and 20 percent in white females.

Data on heart and blood vessel disease in other minority groups are scarce, and most data that are available are derived from limited subgroups. These data indicate, however, that for Mexican Americans, heart and blood vessel disease is a leading cause of death. Although hypertension is less prevalent in Mexican Americans than in black Americans, their rates are still higher than those for whites, especially at lower socioeconomic levels. For Native Americans, preliminary data indicate that coronary heart disease and stroke risk may be increasing, particularly in American Indians residing in urban areas outside the Southwest. Some southwestern American Indians (e.g., the Hopi) show increasing rates of myocardial infarction. Even though coronary heart disease is believed to be relatively uncommon in most southwestern tribes, obesity and diabetes rates are high (particulary among the Pima Indians), and hypertension rates are increasing. These factors are major risks for heart and blood vessel disease in whites and blacks, but whether they increase risk also in southwestern American Indians is not established. For Asian/Pacific Islanders living in the United States, data are so sparse and ethnic derivation so varied that their overall cardiovascular health status is far from clear.

Lung Diseases -- Among lung diseases in the United States, asthma is more prevalent in blacks than in whites, and blacks are twice as likely as whites to be hospitalized for it. The death rate from asthma is more than two times as great among blacks as among whites and is five times as great among black children under the age of 14 years as among white children in the same age range. Sarcoidosis, a chronic, progressive, and generalized disease that primarily affects the lungs, also is more prevalent in blacks than in whites. Mortality statistics show that blacks are at least seven times more likely than whites to die of sarcoidosis.

Blood Diseases -- In the United States, sickle cell anemia, an inherited blood disorder, is predominantly, but not exclusively, found in people of African ancestry. The prevalence of sickle cell anemia within this group is approximately 1 in 500 at birth, affecting more than 50,000 individuals.

Examples of recent advances in programs to improve minority health follow.

Differences in Sodium Transport in Cells May Help Explain Increased Susceptibility of Blacks to Hypertension

Dr. Abraham Aviv, a grantee at the University of Medicine and Dentistry of New Jersey, Newark, is characterizing the transport of sodium and potassium in

skin fibroblasts and vascular smooth muscle cells from blacks and whites with normal or high blood pressure. Recent findings from these studies suggest that differences between blacks and whites involving a cellular sodium transport agent known as the sodium-hydrogen antiport are linked to the regulation of calcium in the cell. Dr. Aviv observed this relationship in skin fibroblasts and plans to follow up his discovery by studying cells from human umbilical arteries of black and white newborns with or without a family history of essential hypertension (hypertension without discoverable organic cause). The hypothesis is that the higher activity of the sodium-hydrogen antiport observed in blacks reflects an increased sensitivity to agents in the body that stimulate both calcium and sodium transport. Since sodium and calcium have already been implicated in essential hypertension, this may help to explain why blacks are more susceptible to hypertension than whites.

Study on Cardiovascular Disease in American Indians Under Way

The Strong Heart Study, initiated by the NHLBI in 1988 in response to a recommendation of the NHLBI Ad Hoc Committee on Minority Populations, focuses on heart and blood vessel disease in American Indians. The objectives of the study are to estimate the morbidity and mortality rates from heart and blood vessel disease among three geographically diverse Indian groups and to measure the levels of risk factors among 1,500 adults, 45 to 74 years of age, in each area. One grantee is studying the Kiowa, Comanche, Apache, Fort Sill Apache, Delaware, Wichita, and Caddo Indians; another is studying the Ogalala Sioux, Cheyenne River Sioux, and the Devil's Lake Sioux; and a third grantee is studying the Pima Indians in the Gila River and Salt River Indian Communities near Phoenix, Arizona. A standardized protocol was developed during the first year of the program. Training of the examination staff was accomplished, and a pilot study of the protocol was completed. Over 600 examinations have been done. A cooperative working relationship with the Indian Health Service and the American Indian communities included in this program has contributed to the progress of the study.

The following investigators are grantees in the Strong Heart Study: Dr. Elisa Lee, University of Oklahoma, Oklahoma City; Dr. Thomas Welty, Aberdeen Area Indian Health Service, Rapid City, South Dakota; and Dr. Barbara Howard, Medlantic Research Foundation, Washington, D.C.

Asthma Self-Management Taught to Hispanic and Black Children

Among the factors believed responsible for the greater occurrence of asthma and asthma-related complications in black and Hispanic populations compared with white populations are lower socioeconomic status, low educational and literacy levels precluding effective self-management practices, inaccessibility and underutilization of health care services, language and cultural barriers between health care providers and patients, nonadherence to treatment regimens, and differences in medical care patterns.

The effectiveness of health education in improving the management of asthma is being tested by Dr. Robert B. Mellins, a grantee at Columbia University, New York, in low-income, urban Hispanic and black families with preschool children who have asthma severe enough to require hospitalization. Families of 435 patients hospitalized because of asthma are identified for one of three treatments: usual care, asthma management training, or asthma management

training plus symptom observation and evaluation training. In other populations, asthma education has been an effective tool in increasing asthma management skills and reducing symptoms of asthma.

Transgenic Mouse Model to Aid Research on Sickle Cell Disease

In a development that opens new avenues for research on sickle cell anemia, scientists have created laboratory mice whose blood cells make human hemoglobin, the protein that carries oxygen throughout the body. This research is described in the separate report on genetic diseases. An animal model containing sickle hemoglobin could be useful in furthering understanding about sickle cell disease and in evaluating therapies for this disorder.

Publication on Managing Sickle Cell Disease Updated

The publication entitled "Management and Therapy of Sickle Cell Disease" has been revised to include topics on surgery and anesthesia, cardiac complications, nursing management, and psychosocial aspects of sickle cell disease. This booklet provides guidance to health care professionals on maintaining health and on prevention and management of complications seen in patients with sickle cell disease. Over 50,000 copies of the first edition have been distributed worldwide.

Directory of Cardiovascular Resources for Minority Populations Added to List of NHLBI Publications Related to Minority Health

The Directory of Cardiovascular Resources for Minority Populations was published in 1989 in response to recommendations of two NHLBI-sponsored Strategy Development Workshops for Minorities. It lists educational materials relevant to cardiovascular health that have been prepared specifically for blacks, Hispanics, Native Americans, or Asian/Pacific Islanders.

ASSISTANCE TO MINORITY STUDENTS AND SCHOOLS

Over the years, the NHLBI has advocated minority involvement in biomedical research by encouraging minorities at all academic levels to participate in the Institute's research training and career development programs. To ensure a sustained level of minority participation, the Institute conducts outreach activities to acquaint minority populations with training and career development opportunities, and the Institute also develops programs to augment existing research training and career development programs of the NIH. Minority training and career development programs supported by the NHLBI include the Minority Access to Research Careers program, Minority Biomedical Research Support program, Minority Institutional Research Training program, and Minority School Faculty Development Award. Recently, the Institute added three Minority Research Supplement programs and the NHLBI MARC Summer Research Training Program to its ongoing activities.

Minority Research Supplement Programs

The NHLBI has initiated three programs to provide supplemental funds to ongoing research grants for support of minority investigators or students who are added to the research teams. To date, the Minority Investigator Research

Supplement (MIRS) program is supporting minority investigators studying, for example, animal aortas after transplantation and marketing research techniques that might overcome existing barriers to participation by blacks in a cholesterol screening program. The Minority Graduate Research Supplement (MGRS) program, a newer program, is supporting a minority student examining the role of certain brain neurons in releasing a hormone that affects blood pressure regulation. The Minority Undergraduate Research Supplement (MURS) program will provide funds to include undergraduate students in heart, blood vessel, lung, and blood research.

NHLBI MARC Summer Research Training Program

The NHLBI MARC Summer Research Training Program offers to MARC (Minority Access to Research Careers) Honors Scholars a 10-week summer research experience in the NHLBI intramural laboratories. During the summer of 1989, seven students (six blacks and one American Indian) from seven different minority institutions participated in the program.

National Cancer Institute

The National Cancer Institute (NCI) has numerous programs to encourage minority involvement in cancer research and treatment programs, and to address the differential burden of cancer in minorities through efforts aimed at cancer prevention, early detection, and treatment.

States Receive Awards to Develop and Implement Cancer Plans

Secretary of Health and Human Services Louis W. Sullivan, M.D. announced the award of cooperative agreements to seven states and the District of Columbia to develop and implement cancer plans designed to meet each area's specific cancer needs. The 7-year awards went to state health agencies in the District of Columbia, Georgia, Louisiana, Maryland, North Dakota, Pennsylvania, Vermont, and Washington State. State health agencies are responsible for underserved populations, and this program directs resources to intervene in populations with specific needs. The eight new awards are in addition to six made earlier to health agencies in Illinois, Nebraska, New York, North Carolina, Texas, and Wisconsin.

National Cancer Advisory Board Calls for Better Access to Information, Prevention, and Early Detection

The National Cancer Advisory Board (NCAB) issued a call-to-action to organizations and individuals to help reduce the cancer death rate. In its recommendations, the presidentially appointed Board noted the health care needs of minority groups, calling for better access to cancer information, cancer prevention, and early detection for those for whom economic disadvantage and indigenous cultural factors impede access to the health care system. Fighting Cancer in America: Achieving the "Year 2000 Goals" outlines the Board's recommendations and summarizes findings from five public hearings it sponsored around the country.

Physicians and Patients Encouraged to Participate in Clinical Trials

Increasing accrual to clinical trials is a major NCI initiative aimed at seeing that important questions about how best to treat cancer are answered quickly and improved treatments are made widely available. The Minority-Based Community Oncology Program is a new cancer control effort to bring state-of-the-art treatment and cancer control research to minorities in their communities by having practicing physicians and their patients participate in clinical trials. A Request for Applications (RFA) was announced and an informal workshop was held for potential applicants. Awards will be made in fiscal year 1990.

Research Programs Target Groups With Elevated Cancer Rates

Numerous research programs target groups with elevated cancer rates and underserved in the areas of cancer prevention, control, and treatment. These groups include, among others, Alaska Natives, Asian Americans, black Americans, Hispanics, Native Hawaiians, the elderly, and the low-income.

For example, two interagency 5-year agreements were signed with the Indian Health Service for a cancer surveillance project for Alaska Natives and for

descriptive and analytic epidemiologic studies on American Indian and Alaska Natives.

Studies are in progress that seek to reduce avoidable cancer deaths, reduce the prevalence of cigarette smoking, and to assess cancer control needs, identify barriers, and develop interventions. Basic research is also under way on cancers where differences are seen in the incidence and biologic aggressiveness of tumors in minority groups, including for cancers of the breast and prostate, multiple myeloma, and adult T-cell leukemia.

Prevention, Education, and Control Activities Include Minority Initiatives

The National Black Leadership Initiative on Cancer, established by the NCAB, is an integral part of the NCI's community-based effort in cancer education, prevention, and control. Six regional coordinators were funded and a project director hired to promote involvement of all segments of the minority community in efforts to reduce cancer death rates.

As part of the NCI's Cancer Prevention Awareness Program for Black Americans, five community-based communication projects were funded in Philadelphia, Detroit, Chicago, Houston, and New York City, to investigate the best ways to involve church leaders, community leaders, and health care providers in educating blacks about cancer prevention, detection, and early treatment.

The NCI signed agreements with the National Medical Association, the oldest national black organization in America, and its Auxiliary, to work together on cancer prevention and control for blacks. Numerous collaborative activities are planned.

NCI Programs Encourage Participation by Minority Researchers

The NCI encourages investigators to involve minorities as research collaborators by providing financial support through the Comprehensive Minority Biomedical Program. Under the Minority Investigator Supplement, 13 minority researchers were funded in fiscal year 1989. The Minority Satellite Supplement provides funds to institutions that serve large numbers of minority patients to support enrollment of minority cancer patients in clinical trials and other treatment programs. Under this activity, 10 medical institutions that collaborate with 17 satellite institutions were funded.

Three cancer centers received funds to expand participation among minorities in cancer control research projects: the University of North Carolina in Chapel Hill, University of Arizona in Tucson, and the University of Southern California in Los Angeles. Five-year awards were made to Meharry Medical College in Nashville, Tennessee, and Texas Southern University in Houston, Texas, to explore ways black colleges can be used as resources to increase cancer prevention awareness in the community.

The NCI "adopted" an inner-city school in the District of Columbia, McKinley Tech High School, and as an intramural program, is conducting activities to encourage the students to pursue careers in science.

National Institute of Dental Research

The National Institute of Dental Research (NIDR) has a variety of activities focused on minority health and assistance to minority students and schools.

Meeting Focuses on Dental Research and Minority Group Issues

As part of its NIDR Long-Range Research Plan for the Nineties, the NIDR convened a meeting of leading minority dental researchers and administrators to describe oral health needs of minority populations in the United States, determine research needs, and identify methods for recruiting minority researchers.

NIDR Embarks on New Initiative in Epidemiology

Recognizing that the epidemiology of oral health diseases and disorders among minorities has yet to be explored systematically and comprehensively, the NIDR initiated a project on "The Oral Health of Racial and Ethnic Minorities in the United States." Led by Dr. Thomas F. Drury, NIDR, intramural researchers are analyzing existing data and identifying new research and action initiatives. Several reports have been published based on NIDR and other Federal data on employed adults, seniors, and U.S. schoolchildren.

NIDR Staff Analyze Oral Health Needs of Minorities

Preliminary analyses of existing databases are elucidating oral health needs of blacks, Hispanics, and Native Americans. Intramural scientists Ms. Janet Brunelle and Dr. Mohandas Bhat have compared the prevalence of dental caries and periodontal diseases for Hispanics living on the East Coast versus those living in the Southwest, for black and other minority children versus white children, and for Hispanic versus non-Hispanic children. Data also have been reported on root surface caries in adults in these same minority groups. Dr. James P. Carlos has documented a very high prevalence of periodontal disease among Navajo children, which has led to action by the Indian Health Service.

Health Promotion/Disease Prevention Efforts Continue

The NIDR supports an active program of outreach and information dissemination to all U.S. population groups, including racial and ethnic minorities. Ms. Alice Horowitz, NIDR, and colleagues design, develop, and disseminate educational materials nationwide through state and local organizations, volunteer groups, health clinics, professional organizations, dental schools and dental hygiene schools, and various Federal agencies. These materials include leaflets, bookmarks, posters, brochures, exhibits, information packets, free-loan films, and educational user guides. Some materials are translated into Spanish.

In 1989, an expert panel on health promotion and disease prevention was convened as part of the NIDR Long-Range Research Plan for the Nineties. Specific strategies for improving oral health education and promotion also are being explored with other organizations and Federal agencies collaborating in the NIDR Research and Action Program for Improving the Oral Health of Adults

and Older Americans. The NIDR is supporting a review of the status of oral health education and promotion programs of several hundred organizations to determine their suitability for distribution to minority and low-income populations. In addition, NIDR staff collaborated with the Bureau of Maternal and Child Health and Resources, HRSA, on a recent PHS Workshop on the Oral Health of Mothers and Children.

NIDR Assists Minority Health Students and Schools

Through the NIDR Minority Research Supplement Program, the Institute provides funds to NIDR-supported principal investigators to increase the number of minorities pursuing research relevant to the NIDR mission. Four awards have been made to date. The NIDR also supports 1 to 3 years of training for minority postdoctoral candidates in the NIH laboratories through the Intramural National Research Service Award Institutional Training Grant Program. In fiscal year 1989, two candidates were selected. To increase awareness about this opportunity, NIDR staff led by Ms. Lorrayne Jackson developed a fact sheet that was disseminated widely. NIDR research and research training support was provided to the historically black colleges of Meharry Medical College, Howard University, and Morehouse College.

The NIDR revised and distributed a brochure on "Opportunities for Minorities in Research" to stimulate interest and increase participation of minority students in scientific research and medicine. An NIDR Resource Collection was established for distributing NIDR surplus scientific books, journals, and slides to minority institutions. To encourage high school students interested in scientific research, NIDR staff participated in several community outreach activities locally. The NIDR also continues to award small grants, regular research grants, and short-term training grants relating to minorities and minority health programs.

Advances Made in Clinical Research Relating to Minorities

NIDR grantees Drs. M. Anne Spence and Rita M. Cantor and colleagues at the University of California at Los Angeles observed that asymmetry in fingerprints correlates with cleft lip and palate in Los Angeles Hispanics, suggesting a predisposition that may be genetic and/or environmental. These formations occur during the same period of embryonic development. Other NIDR-supported studies on the epidemiology and genetics of cleft lip and palate, particularly among Asian populations, also are under way.

Another NIDR grantee, Dr. Harvey A. Schenkein, and his colleagues at Virginia Commonwealth University, Richmond, Virginia, observed that black young people have a stronger immune response than whites to A. actinomycetemcomitans, a harmful bacterium implicated in localized juvenile periodontitis (LJP), perhaps explaining why LJP patients who are black are less likely to develop rampant LJP-related gum disease.

National Institute of Diabetes and Digestive and Kidney Diseases

The rising rate of diabetes in U.S. minority populations is a major public health concern. To reduce the human and economic costs associated with diabetes in blacks, Hispanics, and Native Americans, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is directing special efforts to its research programs.

Diabetes in Blacks

Statistics compiled by the NIDDK's National Diabetes Data Group show that the rate of noninsulin-dependent diabetes mellitus (NIDDM) in blacks is 50 to 60 percent higher than in whites. One in four black women older than 55 has diabetes -- double the rate in white women.

Blacks also experience higher rates of at least three of the serious complications of diabetes: blindness, amputation, and end-stage renal disease (ESRD). The rates of severe visual impairment are 40 percent higher in black diabetes patients than in white patients. Black patients undergo twice as many amputations as do white diabetes patients, and the rate of ESRD is four times higher in blacks with diabetes. These statistics were reported at the NIDDK's National Conference on Diabetes in the Black Population held in September 1988 and cosponsored by the DHHS Office of Minority Health, the Centers for Disease Control, and the American Diabetes Association.

A follow-up conference entitled "Diabetes in the Black Population: Imperatives for Action" was held on March 16-17, 1989, at the Howard University College of Medicine, Washington, D.C. This conference brought together leaders from black professional and community organizations to discuss ways of lowering the incidence of diabetes among blacks and tailoring diabetes messages and community-based efforts.

Obesity is a strong risk factor for NIDDM, the most common type of diabetes and the type that most affects the black population. Dr. David Schlundt of the Vanderbilt University Diabetes Research Training Center (DRTC), Nashville, Tennessee, is investigating patterns of eating behavior in a black obese population where dietary compliance would markedly affect diabetes control. Using computer analysis of data recorded in patient diaries, compliance data, and certain other clinical data will enable investigators to evaluate this technique before recommending it for standard assessment practice in minority diabetes education.

Dr. Wylie McNabb and colleagues at the University of Chicago DRTC, Chicago, Illinois, are developing a program in lifestyle modification in a predominantly black population with NIDDM. The aims of the program are to assist minority groups in changing lifestyles to lose weight and to improve metabolic control of their diabetes.

Diabetes in Hispanics

The rate of diabetes among most Hispanic Americans, the fastest growing minority in the United States, is more than double that of white, non-Hispanic Americans. Data from the Hispanic Health and Nutrition Examination Survey have confirmed that diabetes is a major health problem among American Latinos.

Compared with a rate of 6.1 percent in non-Hispanic whites, the prevalence of diabetes is 13.2 percent in Puerto Ricans, 12.6 percent in Mexican Americans, and 9.2 percent in Cubans.

Dr. Jacqueline Pugh, University of Texas Health Science Center, San Antonio, is studying the potential risk factors for the high incidence of ESRD that has been identified in Mexican Americans in south-central Texas. Factors such as age at onset, type of diabetes, treatment, level of hyperglycemia, hypertension, and urinary tract infections are being compared to those factors in non-Hispanic whites and blacks in the same geographic area.

Diabetes in Native Americans

For 25 years, the NIDDK has maintained a large clinical research effort among the Pima Indians in Phoenix, Arizona, who have a prevalence rate of diabetes that is 10 to 15 times higher than the overall U.S. rate. The results of this research have provided landmark contributions to the state of knowledge about the epidemiology, natural history, and metabolic parameters of NIDDM.

In November 1989, the NIDDK and the Indian Health Service jointly sponsored a workshop that brought together diabetes researchers, the Indian Health Service and Native American and Alaska Native tribes to discuss the present state of knowledge about diabetes and to stimulate the formation of collaborative relationships for new research.

The Kidney Disease of Diabetes Mellitus

Data from the NIDDK's United States Renal Data System (USRDS) demonstrate that blacks constitute 28.1 percent of all ESRD patients, while other minorities represent only 6.1 percent of patients with ESRD.

To focus research on this problem, the NIDDK and Howard University Hospital jointly organized an International Symposium of Renal Disease and Transplantation in Blacks and Minority Ethnic Populations, held on March 29-31, 1989. Scientists and nonscientists exchanged information that reviewed the state of knowledge, identified research needs, and provided new insights to the magnitude of the problem. Discussions of the underlying disease processes and mechanisms of renal diseases leading to chronic renal failure and the multiple problems that the black patient faces concerning renal transplantation demonstrated many avenues for future research.

Minority Research Training

The NIDDK provides funding for two special supplemental awards involving minority scientists and students. These awards are part of the Institute's overall program to strengthen biomedical research and training in institutions with significant commitments to minorities and to increase the awareness and participation of minority scientists in biomedical research.

The Minority Investigator Research Enhancement Award (MIREA) provides support for faculty members of minority institutions to allow them to collaborate with principal investigators with regular research grants funded by the NIDDK. The MIREA program seeks to enhance opportunities for long-term productive collaborations among investigators and eventually to increase the

number of minority investigators who successfully compete for their own research grants.

The Minority Travel Award Program (MTAP) provides additional opportunities for minority students and faculty members of minority institutions to accompany principal investigators currently supported by NIDDK grants to attend national scientific meetings related to the interests of the NIDDK. The purpose of the MTAP is to enhance awareness of biomedical research opportunities among minority students and faculty of minority institutions and to influence more of these individuals to become interested and involved in research and research training.

National Institute of Neurological Disorders and Stroke

Information Dissemination and Outreach Activities

The National Institute of Neurological Disorders and Stroke (NINDS) disseminates information to the minority population on the incidence, prevalence, and treatment of neurologic disorders that have a significant impact on blacks and other minorities. In addition to studying the prevalence of major nervous system disorders in minority communities and reporting these findings to various public and private groups, the NINDS has begun implementing a plan for working with minority media, including American Indian and major black magazines. Additionally, a series of three short articles about stroke research targeted toward black audiences has been drafted.

Research Relating to the Minority Population

The NINDS supports a significant percentage of its AIDS research effort in areas of the country with large numbers of black and Hispanic patients or individuals at high risk for AIDS. Two NINDS grantees involved in the neurologic aspects of AIDS are located in urban areas with large black and Hispanic populations -- Newark, New Jersey, and Miami, Florida. Additionally, studies are being carried out in Baltimore, Los Angeles, and Chicago, where the minority populations show a prominent incidence of AIDS. In addition to supporting research on AIDS, the NINDS is involved in investigations of infant mortality, epilepsy, low birth weight, and diabetes among minority populations.

Stroke in Black Populations

Institute studies of the prevalence of stroke among minority populations are continuing at several institutions. In response to the Secretary's Task Force Report on Black and Minority Health, the Division of Stroke and Trauma of the NINDS requested investigator-initiated research grant applications for support of research that will increase our knowledge and understanding of cerebrovascular disease in blacks and other minorities. Dr. Steven Kittner at the University of Maryland was awarded a Research Career Development Award to study the high incidence of stroke among blacks, and that study is currently in its third year. Additional efforts have begun this year, including another research grant award to Dr. Ralph Sacco at Columbia University in New York City to study the recurrence of stroke in minorities there.

Training and Career Development

Through its Summer Program in the Neurosciences, the Institute is providing short-term training in basic and clinical neuroscience research for minority students contemplating a career in research or academic medicine. During the summer of 1989, 19 minority students -- 32 percent of the total Summer Program group -- were accepted. The NINDS works closely with the directors of neurology and neurologic surgery residency training programs across the country to identify minority candidates for appointments to the various research training positions at the NINDS. Currently, several minority students who began in the Summer Program have returned to the NINDS as scientists following completion of their medical specialization. The Institute has taken great care to publicize this highly successful initiative to the public and in particular to students across the country.

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The Institute, working through the Society for Neuroscience, offers a travel fellowship program which supports the attendance of young minority students and neuroscientists at the annual meeting of the Society. The NINDS cooperates with the Society to sponsor a workshop on research training opportunities in the neurosciences. A similar workshop is held at the American Academy of Neurology's annual meeting.

National Institute of Allergy and Infectious Diseases

The National Institute of Allergy and Infectious Diseases (NIAID) has a long-standing commitment to improving the health status of the Nation's ethnic and racial minority populations through its research programs. Toward that end, the NIAID is striving to develop programs directed at certain minority health problems, to enhance minority health manpower development, and to increase the participation of minority patients, investigators, and institutions in NIAID-sponsored research.

Antigens Unique to Minority Groups Identified Under NIAID Contract

The lack of availability of compatible donor tissues and organs continues to limit the survival of transplants among minority individuals. Matching is complicated by the presence of different antigens and different frequencies of antigens in diverse racial groups. The NIAID has funded two contracts (Dr. Bruce Barger at the University of Alabama, Birmingham, and Dr. Armead Johnson at Georgetown University, Washington, D.C.) intended to identify histocompatibility antigens unique to Native American and black populations. Through these contracts two to three new antigens per year have been identified and others have been characterized. These investigations are vitally important to improve the success of organ transplants in minority populations.

Asthma Education and Therapy Program Planned for Inner-City Baltimore

Asthma is an acute and chronic disease leading the list of childhood diseases causing a significant loss of time from school. In a recent study, NIAID grantee Dr. Floyd Malveaux of the Center for Interdisciplinary Research in Immunologic Diseases at The Johns Hopkins University in Baltimore, Maryland, found that in black males between the ages of 11 and 45, the death rate due to asthma is seven times that of white males. For black women between the ages of 15 and 45, the rate was five times that of white women. The Johns Hopkins group will begin implementation of an educational and therapeutic intervention program in inner city Baltimore aimed at improving the health of these children with asthma and reducing their mortality.

Programs Focus on Increasing Participation of Minorities in Biomedical Research

Several NIAID programs or activities are under way to help increase the number of minority health professionals involved in clinical and basic aspects of research.

The Introduction to Biomedical Research Program is an affirmative action initiative designed to acquaint academically talented minority undergraduate, first-year graduate, and medical students to career opportunities in the broad field of biomedical research. Some of these students may participate in the NIAID Division of Intramural Research Summer Program.

The Intramural Research Sabbatical Program for Minority Scientists provides visiting senior minority scientists with the opportunity to participate in NIAID research.

The NIAID Minority Research Enhancement Program fosters greater awareness and participation of minority scientists by providing supplements to existing

NIAID research grants to include minority investigators in their research endeavors.

AIDS Discussed With Minority Health Care Workers

As part of the continuing efforts to reach minority health care workers with information about AIDS, the NIAID has sponsored workshops and speeches at national meetings of minority health care workers, including the National Medical Association, the National Black Nurses Association, the Fourth Hispanic Medical Congress, and the Third National Conference on HIV Infection and AIDS Among Racial and Ethnic Populations, sponsored by the U.S. Department of Health and Human Services.

National Institute of General Medical Sciences

Minority Access to Research Careers Program

As part of its ongoing commitment to increasing the number of ethnic minorities who participate in biomedical research, the National Institute of General Medical Sciences (NIGMS) supports the Minority Access to Research Careers (MARC) Program. MARC provides research training opportunities for students and faculty at institutions with substantial minority enrollments. With funds from the MARC Program, such institutions can offer grants to train honors undergraduates and enable them to compete successfully for entry into graduate programs leading to the Ph.D. or combined M.D.-Ph.D. degree in a biomedical science. MARC honors undergraduates, who are in their third or fourth year of college, also participate in at least one summer-long research project outside their home institutions. These summer experiences often provide the students with specialized laboratory skills and allow them to coauthor scientific papers. To date, nearly 90 percent of MARC honors undergraduates have gone on to graduate or professional schools.

Other components of the NIGMS MARC Program include fellowships for honors students pursuing doctoral degrees, fellowships for the support of faculty from minority institutions who wish to do pre- or postdoctoral studies, and a visiting scientist program that encourages outstanding teacher-scientists to serve as faculty at minority institutions for periods ranging from 3 to 12 months.

The excellence of the MARC Program was attested to in a 1988 report of the Congressionally mandated Task Force on Women, Minorities, and the Handicapped in Science and Technology, which singled MARC out as "a prime example of a successful Federal intervention program" designed to "give minorities and women access to science and engineering."

Minority Research Supplements Program

In addition to its MARC Program, the NIGMS is also deeply involved in the recently established NIH-wide initiative aimed at increasing the number of minority individuals (including high school students) who participate in ongoing research projects. In the first few months of this program, NIGMS received 26 applications from current grantees requesting supplements to support graduate students, undergraduate students, or postdoctoral fellows on their projects. Of these, 15 awards were made, primarily to graduate students but also to undergraduate college students and to minority investigators.

National Institute of Child Health and Human Development

Infant mortality is highest among babies born to minority and low-income women. A special program of the National Institute of Child Health and Human Development (NICHD) is addressing health problems relevant to these populations. Through rigorous prevention research, educational activities, and health promotion interventions, it is hoped that maternal and child well-being will improve.

Study Seeks to Identify Factors Associated With Delivery of Low Birth Weight Infants

Dr. Heinz Berendes of the NICHD Prevention Research Program has carried out a study to identify factors associated with the delivery of low birth weight infants in the District of Columbia. Interviews were conducted with 500 black mothers of low birth weight infants and 500 black mothers of normal birth weight babies delivered at the same hospitals during 1984-1985. Risk factors being investigated include past medical and family histories, socioeconomic status, and nonprescription drug use, including alcohol, tobacco, caffeine, and illicit drugs.

Among the results of this study, Dr. Berendes learned that in spite of the fact that cigarette smoking during pregnancy is the number one preventable cause of low birth weight, a large proportion of women continue to smoke during pregnancy. In this study group, 57 percent of the women who delivered low birth weight babies and 39 percent of those who delivered normal birth weight babies reported smoking during pregnancy.

NICHD Developing Smoking Modification Program for Pregnant Women

As a result of these findings, the NICHD is presently developing a smoking cessation intervention program to help women modify their smoking behavior during pregnancy. Dr. Leslie Cooper from the Prevention Research Program of the NICHD has carefully designed a program that will appeal both to physicians and patients. A multimedia package of materials, including questionnaires, pamphlets, and videotapes of fetal development, will be given to women as part of the project that is scheduled to begin soon in the District of Columbia with a small number of participating physicians. After a thorough evaluation of the pilot study, the program will be expanded.

Also participating in this project are the National Cancer Institute, National Heart, Lung, and Blood Institute, Centers for Disease Control, American College of Obstetricians and Gynecologists, American Cancer Society, and American Lung Association, as well as numerous other organizations, researchers, experts, and physicians.

National Eye Institute

More than 2 million adult Americans have glaucoma, an eye disease that can cause blindness when an elevated fluid pressure in the eye damages the optic nerve. Glaucoma is the leading cause of blindness among black Americans. Although blindness in the black population appears to be much higher than it is in the white population, the exact difference has never been firmly established.

Two Studies Focus on High Rates of Glaucoma Among Blacks

Recognizing that interventions to reduce the glaucoma risk among blacks must be based on accurate, population-based data, the National Eye Institute (NEI) has inaugurated two studies to improve this information base. The goal is to determine why blacks have such a disproportionate risk of visual loss from glaucoma and to develop measures to reduce this risk.

Scientists conducting the NEI-sponsored Baltimore Eye Study have been investigating the prevalence and severity of glaucoma and other eye disorders among blacks and whites who live in clusters of racially mixed, urban areas of East Baltimore. The investigators are gathering data on 2,395 blacks and 2,913 whites age 40 and older.

Early results show that, compared with whites, blacks in the study had higher rates of glaucoma at all ages and developed glaucoma at lower intraocular pressures. The prevalence of glaucoma in the blacks was 4.7 percent compared to 1.7 percent in the whites. The prevalence of blindness was 1.6 percent for blacks and 0.89 percent for whites. The incidence of glaucoma did not rise appreciably among whites until age 65, but the increase among blacks was steady beginning at age 40.

This type of information is important in the design of intervention strategies. For example, recommendations on what age glaucoma testing should begin may need to be different for blacks and whites.

Another NEI-funded study is investigating the prevalence of glaucoma in a Caribbean black population. The Barbados Eye Study will determine the prevalence of glaucoma in the island blacks and identify factors that will improve methods for early detection and treatment. Preliminary data from Barbados indicate that 13 percent of the island's black population over age 54 have glaucoma.

Both of these studies will continue to examine why blacks, compared with whites, have a higher risk for glaucoma.

National Institute on Aging

The National Institute on Aging (NIA) supports biomedical, social, and behavioral research and training related to aging processes, diseases common in old age, family care for dependent older people, and other special needs of the older population. The Institute is especially interested in research to improve the health and longevity of minority populations. Specifically, the NIA studies cultural influences, life expectancy, health status, environmental influences, family structure, social networks, and problems associated with life transitions as they relate to black, Asian/Pacific Islander, Hispanic, and Native American minorities.

Older Blacks Have Variety of Support Networks

It has long been known that older people frequently turn to family members for aid in times of trouble. Yet, disproportionately high rates of poverty, poor health, and single-parent families place especially heavy burdens on black families just to maintain everyday lives. With these demands and strains within black families, to whom do older blacks turn for help?

As one example of research focused on minority populations, NIA grantees Drs. Robert Joseph Taylor and Linda M. Chatters at the University of Michigan in Ann Arbor and Dr. Vickie M. Mays at the University of California at Los Angeles examined data from the 1980 Panel Study of Income Dynamics (a well-known, long-term study of family economics). This survey asked a representative sample of family members to whom they would turn for assistance during an extended time of trouble. Respondents ranged from 19 to 94 years of age; 20.7 percent were 56 or older. Dr. Taylor and his colleagues analyzed the 2,533 responses of blacks. Results showed that black Americans have developed a variety of networks for support that include and extend beyond the immediate family.

Many similarities in helper networks were found among all population groups. For blacks, as well as for non-minority older people, the parent-child bond appears to be of primary importance. Being able to turn to adult children in an emergency is considered most important for all older people. Additionally, this study confirms that widows from all ethnic groups seem to have comparatively fewer sources of assistance and frequently rely on distant relatives or non-kin.

Racial differences in informal networks show blacks less likely than whites and Hispanics to mention in-laws as a source of help; they were, however, more likely to mention siblings and aunts or uncles. More than 20 percent of the black participants cited non-family members as important sources of support. According to Dr. Taylor and colleagues, support from the church or neighbors may be especially important for rural blacks whose adult children have migrated to cities.

As the population of older Americans grows and the proportion who are minorities increases even more rapidly, many of the responsibilities for assisting older relatives will fall on the shoulders of family members. In black communities, a clear understanding of how family and friends can function as a helping network is necessary to develop realistic policies. Advance planning can strengthen the success of these efforts and allow older people to maintain their independence for as long as possible.

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Since its creation in 1986, the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) has conducted and supported research related to the health problems of minorities, particularly the rheumatic diseases systemic lupus erythematosus and ankylosing spondylitis and the skin disease vitiligo. The NIAMS also has encouraged minority involvement in research careers through its participation in the NIH-wide programs and through the development of special initiatives. These include the Minority Investigator Research Enhancement Award, which was designed to provide research experiences for faculty of minority institutions, and the Minority Travel Award Program (MTAP), which enables minority students and faculty from minority institutions to attend national scientific meetings.

Rheumatic Disease Risk Factors Identified

Systemic lupus erythematosus is a potentially serious, inflammatory connective tissue disease that can affect many different organs of the body in varying combinations, including the skin, the joints, the kidneys, the brain, the lungs, and the heart. The disease tends to affect women in their childbearing years. Black women are three times more likely to develop lupus than are white women. Asians, certain Native American tribes, and Hispanics also appear to be at increased risk. The NIAMS conducts and supports a considerable amount of basic, clinical, and epidemiologic research on the disease. There appears to be some genetic predisposition to lupus based on studies in twins, families, and populations. Genetic markers for lupus were recently studied by researchers led by NIAMS grantee Dr. John Reveille, University of Texas Health Science Center, Houston. The investigators looked at a variety of immune system regulating genes in 79 black lupus patients and 68 healthy black controls. They were able to identify a strong genetic risk factor -- a type of C4A gene deletion associated with certain HLA antigens -- that may predict lupus susceptibility in black Americans.

The NIAMS has convened an ad hoc Task Force on Lupus in High Risk Populations to develop educational interventions that may improve the outcome of lupus in these populations. It is currently focusing on developing materials and messages for young black women and health professionals who serve them.

Ankylosing spondylitis is a form of spinal arthritis that can cause progressive stiffening of the back. It is strongly associated with the genetic marker HLA-B27. This marker appears to be much more frequent in certain Native American populations than in the general population. The NIAMS is supporting an epidemiologic study of this disease in Eskimo populations where the frequency of HLA-B27 is approximately 20 to 40 percent.

Direct Evidence Found for Autoimmunity in Vitiligo

Vitiligo is a common pigmentation disorder that results in patchy loss of skin color. it occurs in 1 percent of the population and afflicts all ages, all races, and both sexes. Loss of skin color can be emotionally devastating to dark-skinned individuals in particular. The underlying mechanism of the disease has been studied with NIAMS support by a research team including Dr. Jean Claude Bystryn at the New York University School of Medicine, New York

City, and colleagues at the University of Colorado School of Medicine in Denver. The researchers applied serum (blood) samples from patients with active, progressive vitiligo and from normal controls to cultures of human pigment-producing cells (melanocytes). Cell damage occurred in cultures where the vitiligo sera had been added. The researchers say that this is the first direct evidence that vitiligo is an autoimmune disease, in which normally disease-fighting antibodies are produced against body tissues.

Additional research results in the rheumatic diseases are described in the separate report on arthritis, rheumatic diseases, and related disorders.

Division of Research Resources

The Division of Research Resources (DRR) supports several programs aimed at increasing the representation of ethnic minorities in biomedical research. These same programs are adding information helpful in improving the health of minorities in the United States.

Research Centers for Minority Institutions Program

The DRR administers the Research Centers for Minority Institutions (RCMI) Program on behalf of the NIH Office of the Director. The RCMI Program is designed to expand the nation's capacity for the conduct of biomedical and behavioral research by providing grant support for predominantly minority institutions to develop and/or expand their research infrastructure. RCMI awards are used to augment the research environment at these institutions, strengthening both the physical and human resources.

In fiscal year 1988, more than $11 million in RCMI funds were awarded to 17 colleges and universities. The awards were used to develop core laboratories, recruit faculty members, upgrade research facilities and support specific pilot research projects, many of which focused on minority health issues.

Minority Biomedical Research Support Program

The Minority Biomedical Research Support (MBRS) Program awards grants that strengthen the research capabilities of minority institutions and the involvement of faculty and minority students in research. MBRS funds help these institutions, mostly 2-year and 4-year colleges, universities, and health professional schools, establish and improve the research capability of their faculty and develop their research facilities. By increasing the research capabilities of grantee institutions, MBRS awards encourage minority faculty and student participation in biomedical research.

In fiscal year 1988, the MBRS program awarded $39 million to more than 90 minority institutions. Funding supported 1,095 undergraduate and 407 graduate positions. Included in the $39 million were more than $10 million awarded to these institutions from other bureaus, institutes and divisions of the NIH, as well as the Alcohol, Drug Abuse, and Mental Health Administration to co-fund research projects.

Minority High School Student Research Apprentice Program

The Minority High School Student Research Apprentice (MHSSRA) Program, which is part of the DRR Biomedical Research Support Program, encourages minority high school students to pursue careers in biomedicine, health research, and the health professions.

In fiscal year 1988, the MHSSRA Program awarded almost $1.7 million to 323 institutions, which offered 8-week apprenticeships to high school students. Most were summer positions, although some continued during the school year. At the Beth Israel Medical Center in New York City, four apprenticeships were set aside during the school year for participation in AIDS risk-reduction research. High school students assisted the scientists in data analysis.

Minority Health

Many of the research projects supported by the MBRS and RCMI programs are focused on minority health problems. One example is the work by RCMI grantees at the Charles R. Drew University in Los Angeles, California, who are using a noninvasive cardiovascular recording technique to study the physiologic stresses that injure the fetus. Estimates indicate that 27 percent of the excess mortality among black Americans occurs during infancy.

RCMI funds helped the Charles R. Drew University recruit and hire Dr. Edward H. Hon, who developed the recording technique. This technique detects minute changes in cutaneous blood pressure patterns obtained with miniature pressure transducers mechanically coupled to the skin overlying the finger tips. Dr. Hon and his colleagues are now using this technique to study pregnancy-induced hypertension and preterm labor in the hope of developing more effective ways to detect and treat high-risk women. With this simple screening test, the grantees found distinct changes in the cutaneous blood pressure patterns in many high-risk patients.

In a study of 120 high-risk patients, Dr. Hon and his colleagues learned that significant vasoconstriction, indirectly reflected by cutaneous blood pressure patterns, is associated with a lower than normal birth weight averaging about 2,660 grams. If vasoconstriction is normal, average birth weight is about 3,120 grams.

National Center for Nursing Research

The National Center for Nursing Rsearch (NCNR) is providing many opportunities for increased minority participation in nursing research.

The NCNR encourages institutions with current Institutional National Research Service Awards (NRSA) to request administrative supplements to recruit and train minority students. Two such supplements have been made to date to support three minority trainees in fiscal year 1989, and additional trainees in future years. All competing applications for Institutional NRSAs must include plans to recruit and train minority nurses.

Research supplements for minority undergraduate students, graduate research assistants, and minority investigators are available with Research Project Grants, Program Project Grants, Specialized Center Grants, and Cooperative Agreements. To date, the NCNR has funded one such supplement, and hopes to support others in the future. Specialized Center Grants require plans for recruiting and training minorities in research and linkages with minority nursing faculty.

The NCNR also supports research on factors associated with increased health risks in minority populations, including socioeconomic status, access to health care, and cultural differences in health beliefs and practices. Following are two examples of NCNR-supported studies on minority populations.

Nurses in Black Churches Teach Members About High Blood Pressure

NCNR grantee Dr. Eva Smith of the College of Nursing, University of Illinois in Chicago is developing and evaluating programs in black churches to help members with high blood pressure manage the disease.

Dr. Smith and her colleagues are training nurse members of twenty black churches in Chicago to conduct group instruction for hypertensive members of their congregations about managing medications prescribed by their doctors and about diet, exercise, stress reduction, and other lifestyle changes that can help control the disease. The investigators will compare blood pressure, weight, dietary habits, and knowledge about the disease before and after the 8-week training sessions, to look for improvement in these areas. About 200 people are expected to attend the twice-weekly group sessions.

Nurses trained to conduct the education and support sessions are expected to teach other nurses to conduct similar sessions with other groups. Dr. Smith expects that the educational programs in the churches will continue to grow and benefit the people in the community after the research phase is over.

Researchers Study Aspects of Health and Aging in Older Hispanics

Dr. Rita L. Ailinger of the School of Nursing, George Mason University, Fairfax, Virginia, is assessing changes in physical and mental health, socioeconomic resources, and utilization of health and community services among 152 Hispanic older people who participated in a study of these factors 5 years ago. She will be looking for socioeconomic factors that may relate to declines in function in these older Hispanics. Dr. Ailinger also will assess the increase in use of health and human services among Hispanics 75 and older. In

addition, she is studying cultural concepts of health and aging and traditional views toward medical treatment among these Hispanics that may affect their responses toward medical treatment in this country.

Developing a better understanding of cultural factors that affect health and aging among Hispanics in the United States can help nurses and other health care workers develop more successful health services for these groups.

Outlook

It is hoped that the programs of the NIH will result in improved health and easier access to biomedical research careers for minorities. One immediate outcome of importance has been the increased communication and cooperation between the NIH and minority groups from academic institutions and public and private organizations. This cooperation will continue to be essential in efforts to reach minority populations with health information and health care, as well as to attract minority students to careers in biomedical research.

ALCOHOL, DRUG ABUSE AND MENTAL HEALTH ADMINISTRATION

National Institute on Alcohol Abuse and Alcoholism

MINORITY HEALTH AND ASSISTANCE TO MINORITY HEALTH STUDENTS AND SCHOOLS

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) supports the training of minority students for careers in alcohol research, and supports activities both to encourage the involvement of minority investigators in alcohol research and to stimulate interest in research of special concern to minority populations. In addition, the research programs of the Institute include studies in which there is a strong focus on alcohol problems among racial and ethnic minority groups and communities.

NIAAA's Minority Alcohol Scholars Program supports four scientists through grants for the conduct of research on minority issues and the development of research capability among minority scientists. Typical activities of the Scholars include the development of state-of-the-art reviews, analysis of existing data sets, and critical reviews of literature for publications. In addition, they conduct seminars, and organize scientific conferences.

NIAAA also provides support to the Minority Biomedical Research Support Program administered by NIH by funding alcohol-relevant components of larger research projects. The goals of the program are to increase and strengthen minority research capacity, and to increase research involvement of minority students, faculty and institutions. Currently supported projects are investigating the neuropharmacology and neurobehavior of ethanol tolerance; chronic ethanol ingestion and interactive effects of nicotine; alcohol and blood vessels; alcohol effects in the developing central nervous system; pulmonary ethanol metabolizing system; and effects of maternal alcohol consumption during pregnancy.

NIAAA provides support for the Minority Access to Research Careers (MARC) program for honors undergraduate training. The program is administered by the National Institute of Mental Health and provided 13 awards in FY 1989, 5 of which were to Historically Black Colleges and Universities (HBCU). The program assists institutions with a substantial enrollment of ethnic minority students to enhance opportunities to recruit outstanding minority individuals into careers in science. The primary objective is to increase the number of students who are academically prepared to be successful in doctoral level programs. NIAAA will also provide support for the MARC Sixth Annual Colloquium to be held in March 1990. The colloquium provides opportunity for MARC students to present their research findings to other students and faculty of MARC programs; to participate in other activities including workshops and recruitment events; and to interact with scientists representing a range of disciplines and research areas. NIAAA also participated in the first meeting of MARC Program Directors in

December 1989. The meeting marked the tenth anniversary of the MARC program.

NIAAA has established an Institute committee to plan and carry out activities to encourage greater participation of Historically Black Colleges and Universities (HBCU) faculty in NIAAA programs. Membership includes representatives from operating units of the Institute, including extramural and intramural programs, policy and scientific affairs offices. NIAAA's plans for FY 1990 include staff visits to HBCUs to discuss opportunities in the alcohol research field; technical assistance for preparation of grant applications; identification of black researchers, especially from HBCUs to serve on scientific review committees; and dissemination of information about research training opportunities available in NIAAA intramural and extramural programs.

In 1989, NIAAA and NIDA issued a program announcement soliciting administrative supplements to existing extramural research grants to support research by minority researchers or researchers studying issues that impact on minority populations. Through this mechanism, increased support will be provided to minority scientists and other researchers to expand scientific knowledge about alcohol's effects on health, to gain research experience, and to increase their commitment to examining problems of alcohol abuse among racial and ethnic minority groups. Response to the program has been positive and two supplementary awards were made in 1989. A more recent announcement issued by the three ADAMHA institutes provides opportunity for support that will enable minority institutions to increase their capacity to conduct research in alcohol, drug and mental health fields.

Recruitment and training that prepares minority individuals for research careers has been a high priority program objective in NIAAA. Considerable progress has been realized through consistent encouragement of senior alcohol investigators and project directors together with maximum utilization of research training resources. For example, one of the Alcohol Research Centers in conjunction with the University's Office of Minority Affairs and the National Center for American Indian/Alaska Native Mental Health Research, sponsors summer research projects for six American Indian college students. There are plans to expand this program to include Hispanic and black students.

Through its extramural research programs, the NIAAA supports epidemiologic studies that focus on alcohol use patterns and alcohol abuse problems among different racial and ethnic groups. Much has been learned about how cultural diversity is related to medical, psychological and environmental factors that affect prevalence and distribution of alcohol-related health problems among minority populations. Some of this emerging knowledge base is captured in two recent NIAAA publications, NIAAA Research Monograph 18 entitled "Alcohol Use Among U.S. Ethnic Minorities" and NIAAA Research Monograph 19, "Cultural Influences and

Drinking Patterns: A Focus on Hispanic and Japanese Populations." A variety of collaborative and creative approaches are being utilized to further advance research in minority relevant issues involving analyses of existing large-scale data sets which contain measures of alcohol use and alcohol diagnosis among Mexican Americans in household populations. Seven studies are supported through grants awarded by the extramural epidemiology program. Three intervention-focused projects are supported by the prevention research program. Each has a unique study population, Indian women in Mexico, urban American Indian adolescents, and Mexican-American families. Findings from these studies will be useful in developing age and gender specific, culturally appropriate prevention strategies to reduce alcohol-induced problems. In addition, two Alcohol Research Centers are conducting studies which focus specifically on minority aspects of epidemiology and prevention.

Some studies in the fetal alcohol area have reported findings which suggest that offspring of black women may be particularly susceptible to adverse consequences of prenatal alcohol exposure. Progress in this area continues as new studies have been designed to specifically examine a wide array of variables and researchers have been able to recruit populations representing minority groups. The NIAAA Alcohol Research Centers (ARC) program supports a multidisciplinary, integrated program of research to explore preventions of and mechanisms related to alcohol-related neurobehavioral deficits. In these studies, as well as in those conducted by the project's senior investigators in their earlier preliminary work, mother-infant patients live in the inner city, are predominantly black, extremely disadvantaged, and at high medical risk. Another new project is a prospective study designed to examine children, who have reached school age, for developmental outcomes and possible concomitant effects of prenatal and postnatal maternal alcohol abuse. This study has some unique features in that the mothers and children in the sample represent a predominantly black population and have been involved in earlier studies and programs; thus baseline data on many health parameters are available to investigators.

National Institute on Drug Abuse

MINORITY HEALTH

Drug abuse disproportionately affects minority groups. Adverse consequences suffered by minority populations include negative effects on employment, school achievement, and family stability as well as increased morbidity and mortality. Racial, ethnic, and cultural factors are likely to influence virtually every area of drug abuse, including the initiation of drug use, the choice of drugs, the nature and extent of peer influence on drug use, the "style" of abuse (i.e. route of administration, frequency, and pattern of use), perception of drug abuse treatment (e.g. its availability, accessibility, and effectiveness), and relapse to drug use after treatment. Both prevention and treatment programs must reflect the ethnicity of the community which they serve if they are to be effective.

NIDA's National Household Survey estimates that 3.7 million Hispanics and 7.6 million blacks, aged 12 and older, have tried an illicit drug in their lifetime. An estimated 1.3 million Hispanics and 3.2 million blacks currently use an illicit drug. Hispanic teenagers aged 12-17 years are more likely than white or black youth to have used cocaine; in contrast, blacks age 35 and older are more likely than whites or Hispanics to have used cocaine. Alaskan Natives and American Indians in Alaska are more likely to have tried an illicit drug than other racial/ethnic groups in the state.

Health Consequences of Drug Abuse for Minority Populations: Potential negative health-related consequences of drug abuse include overdoses, hepatitis B infection, bacterial endocarditis, AIDS, and other sexually transmitted diseases. Drug abuse may increase the risk of homicides and crime, accidents and injuries, Parkinson-like syndrome, obstetric complications, adverse birth outcomes, as well as suicide and psychiatric problems.

Drug abuse related emergency room cases provide one measure of the morbidity associated with drug abuse. Data from the Drug Abuse Warning Network (DAWN) shows that Black and Hispanic patients are more likely than white patients to mention an illicit drug--heroin, cocaine, marijuana, or PCP--in conjunction with an emergency room visit. Hispanics accounted for 22 percent of emergency room episodes due to inhalants, a rate significantly disproportionate to their numbers in the total population (8 percent).

While the percentages of cocaine emergency room mentions greatly increased for blacks and whites from 1984 to 1987, cocaine-related deaths among blacks and other minorities tripled during this period, compared with a doubling among whites. Between 1984 and 1987, the percentage of black males mentioning cocaine increased from 19 percent to 51 percent, and rates for black

females increased from 12 percent to 41 percent. Comparable figures for white males and females during the same period were 11- to 27 percent (males) and 5- to 13 percent (females). While whites are more likely than blacks or Hispanics to concurrently combine drugs, blacks and Hispanics are disproportionate users of dangerous drugs, i.e., drugs that are more likely to cause adverse health consequences, including death. The percent of black males who mentioned heroin showed a large decline between 1984 and 1987 (33 percent to 20 percent); still, more blacks died of heroin-related causes than whites or Hispanics.

Black clients admitted to treatment for cocaine abuse are more likely than white cocaine abusers to inject or freebase the cocaine. In addition, black and Hispanic clients in treatment for drug abuse are more likely to report "speedballing" (intravenous combination of heroin and cocaine).

Social Issues: Persons at high risk for drug abuse are often raised in an atmosphere filled with social and psychological pathology: poverty, illiteracy, malnutrition, delinquency, violence, emotional deprivation, mental illness, and alcohol or other drug dependence. While these unhealthy environmental conditions often exist prior to an individual's becoming drug-dependent, they are exacerbated by problems associated with drug dependence.

Drug abuse may also have negative effects on employment, school achievement, socioeconomic status, and family stability. NIDA plans more studies in this area, but what is known now suggests that the adverse consequences of drug abuse may be greater for minority populations.

AIDS: Blacks and Hispanics, 19 percent of the U.S. population, are over-represented in total AIDS cases and among intravenous drug abusers where, together, they account for 76 percent of the total intravenous drug abusing related AIDS cases. Blacks constitute 50 percent, and Hispanics 29 percent, of the AIDS cases among heterosexual intravenous drug abusers. The impact on minorities of AIDS associated with intravenous drug abuse is also reflected in cases of AIDS among their heterosexual partners and newborns. Eighty-five percent of the AIDS cases who were heterosexual partners of intravenous drug abusers are black or Hispanic. Eighty-five percent of non-white children with AIDS acquired the disease from a parent who is an intravenous drug abuser or who is the sexual partner of an intravenous drug abuser; only about 51 percent of white children have perinatally acquired AIDS.

Although inadequate data on risks factors for adolescent AIDS are available, blacks and Hispanics make up more than half of all current adolescent AIDS cases. Moreover, HIV seropositivity among black military recruits was four times higher than among white recruits.

Data from a New York City study suggest that blacks and Hispanics engage in more frequent sharing of needles with strangers in shooting galleries. Furthermore, blacks who stopped using needles did not do so until later in the AIDS epidemic than whites. These findings raise the possibility that the environmental setting where drug use occurs may explain racial/ethnic differences in seroprevalence rates. Racial/ethnic differences in intravenous cocaine use, number of intravenous drug abusing sex partners, and number of paying sex partners are being explored as possible explanations for some of the seroprevalence differences.

Crime: The findings from a recently completed NIDA-funded study on the criminal activities of 285 adult female and male active narcotic addicts living in New York City suggest that Hispanic and black addicts are more likely to be arrested for or to report committing certain types of crime more often than white addicts. Hispanic men and women addicts, particularly, were more likely to report involvement in drug dealing and to be arrested for prostitution than black or white drug addicts. Black drug addicts were more likely than white or Hispanic addicts to be arrested for aggravated assault and as likely as Hispanic addicts to report involvement in drug dealing.

Minority Adolescents and Drug Abuse: The effect of drug abuse on dropping out of school has not been fully documented, but drug abuse among both dropouts and their families is considered a significant factor. Several NIDA studies are in progress that examine the effects of drug use on rates of dropping out of school in minority communities. Initial data from an ongoing 3-year study of drug abuse among Mexican American dropouts indicate that some of the variables that distinguish dropouts from others are: skipping school, wider age spread among best friends, consorting with other dropouts, hating school, hating their teachers, bad grades, and drug use.

Another NIDA-funded study is examining the etiology of substance abuse within a high risk black youth population: inner city, male teenagers, high-school dropouts, and unemployed. These youth were, on average, 17 years old and generally had dropped out of school before the tenth grade. About 25 percent reported using illicit drugs at least once a day. Four factors related to high levels of substance abuse stood out. 1) the occurrence of negative life events in the youth's life during the past year, such as the death of a close family member; 2) an absence of help and support from others in coping with stress; 3) features of the youth's relationship with his father, e.g., growing up fatherless or lacking the father's emotional support; and 4) no involvement in meaningful activities in the community. Youth who reported participating in activities that helped other people and contributed to the goals of a community group were less likely to abuse drugs.

Minority Training: An important part of drug abuse research is the provision of adequate numbers of appropriately trained minority researchers. In support of recommendations made by the Secretary's Task Force on Black and Minority Health, NIDA has developed Special Populations Research and Training Programs that include support for: 1) targeted research grants support for MARC, MBRS, Minority Supplemental Research Awards, and AIDS training; 2) grants technical assistance and support for research training and research grants submitted by special populations researchers and others interested in examining drug abuse among special populations; 3) evaluation of special population research; and 4) publication of research and clinical findings related to drug abuse among special populations.

The Special Populations Research Development Program provides scientific and methodological mentoring to ethnic minorities, women and other special population Ph.D.s and M.D.s seeking to engage in drug abuse research activities. These efforts concentrate on developing statistical an analytical skills, identifying and validating research instruments and methods, and other research and laboratory techniques. Of those completing the program, 80% have submitted grant applications. Subsequently, 80% of these applications have been funded by NIDA and other ADAMHA Institutes. Among these grants are studies that examine drug abuse issues among the homeless minorities; American Indians and Hispanic adolescents and young adults, inner city unemployed Black youth, and minority groups at risk for AIDS.

Office for Substance Abuse Prevention

MINORITY HEALTH AND
ASSISTANCE TO MINORITY HEALTH STUDENTS AND SCHOOLS

The programs funded by the Office for Substance Abuse Prevention are structured to be sensitive to minority drug and alcohol prevention needs. The majority of OSAP-funded activities serve to enhance prevention strategies, programs, and services in minority and multicultural communities. However, support also is provided to minority health schools and minority health students, principally through ADAMHA's Historically Black Colleges and Universities (HCBU) Initiative. In addition, OSAP awarded high-risk youth demonstration grants, in FY 1987, to three HCBUs: Edwards Waters College, Jacksonville, FLA; Coppin State College, Baltimore MD; and Southern University, Baton Rouge, LA.

OSAP has provided support for faculty members from HBCUs such as Coppin State College (MD), Morehouse (GA), Norfolk State (VA), Meharry Medical College (TN), and Central State (OH), to participate in substance abuse prevention program planning activities for high risk communities.

OSAP is currently developing a National telecommunications conference on drug abuse prevention, to be held during FY 1990, at the Cork Institute on Black Alcohol and Other Drug Abuse, that will be hosted by the Morehouse University School of Medicine in Atlanta for HCBUs using the HCBU satellite network.

National Institute of Mental Health

MINORITY HEALTH AND ASSISTANCE

RESEARCH:

The unique social, cultural, and historical backgrounds and characteristics of minority populations makes their mental health needs especially complex. Furthermore, the perception and definition of mental illness, its identification and treatment, the spectrum of support mechanisms, the availability, appropriateness and accessibility of such mechanisms, help seeking behaviors and the interaction with service providers are some of the factors which affect the outcome of mental illness. Minority population responses to these factors provide a spectrum of issues worthy of investigation towards improving services delivery, including prevention and intervention strategies.

For support of mental health research, NIMH uses several types of funding mechanisms: small grants, regular research grants, First Independent Research Support and Transition Awards, program project grants, cooperative agreements, and clinical research center grants among others. Research awards are awarded to institutions on behalf of principal investigators who have designed and will direct a specific project or set of projects. Stimulation and support is available to investigators to study clinical, applied, and basic science issues relevant to minority groups. The importance of minority research within the total research agenda of the NIMH is incorporated and reflected in each Division's research portfolio. Support for minority studies from these portfolios continues to be a major priority and commitment of Institute staff and policy.

Research priority areas such as minority services research have been addressed through the use of national workshops such as those recently held in Hawaii, Austin and forthcoming in Washington, D.C. These forums provide an opportunity for senior investigators in the field to present their research findings as well as to explore opportunities to develop collaborative research projects.

Technical assistance is provided to junior researchers to stimulate and enhance the capability and capacity of researchers in pursuing minority mental health research grant support. A variety of mechanisms are being used including: distribution of informational packages on program priorities, grants mechanisms, and application procedures; critiques of draft proposals. To further assist promising researchers conducting mental health services research on minorities, the Division of Biometry and Applied Sciences has initiated a prototype experimental Technical Assistance Program for minority researchers. Phase I of this program was comprised of a workshop which provided basic orientation to the grants application process and the theoretical and applied aspects of minority mental health services research. Phase II of this effort will be to

provide intensive individual research consultation by services research experts to seven most-promising researchers. The consultation process will be followed by a mock research application review and eventual submission of research applications. The ultimate outcome will be the increased number of approved, fundable mental health services research grants.

Further minority research is performed under the auspices of national Minority Mental Health Research Centers which were developed to design, conduct, and implement research and research development programs relevant to minority groups. It is expected that within this context, the Centers will provide a setting for the training of minority students as researchers. These centers are problem-oriented, comprehensive and integrative as well as multi-disciplinary in their approach. Currently, there are four such Centers. Each Center has a clearly defined set of research foci or set of scientific problems of major importance to the understanding of a specific minority group. The Centers maintain a research environment wherein hypothesis development and testing can unfold in the context of both pilot and follow-up studies, and where new methodologies and data-gathering techniques can be formulated, developed and tested. The recent re-issuance of the Minority Mental Health Research Centers announcement has generated significant interest in the minority research community. It is expected that up to four new research centers will be funded. The objective is to strengthen and expand the number of national centers capable of generating and conducting multi-disciplinary research on the mental health needs and issues of minority populations.

Some examples of investigator-initiated regular research grants on minority populations come from the NIMH prevention research program and the AIDS research program.

A prevention research intervention by Leila Beckwith at UCLA is studying the prevention of cross generational transmission of poor parenting in low income, disrupted families by focusing on increased maternal involvement and responsive interactions with their sick pre-term infants during the first year of life.

The intervention appeared to unhook maternal behavior from predisposing adverse factors. Women who showed ambivalence or rejection of their pregnancies by not getting prenatal care were able, with intervention, to show high involvement with their infants. Women who themselves had grown up in abusive, alcoholic, or disrupted families were able, with intervention, to engage in increased reciprocal interactions with their infants. In addition, mothers became more realistic about their own lives and expectations of their infants. Differences in infants' play and cognitive development associated with intervention began to emerge at 13 months, and became stronger by 20 months.

University of Pittsburgh researcher Larry Michelson found that children at risk for conduct disorder who participated in a 2-year

prevention intervention showed a decrease in parent reported antisocial behavior and child reported symptoms. Children also demonstrated a decrease in the process of negative attributions which have been associated with antisocial behavior. The investigation evaluated a Cognitive-Behavioral prevention program designed to improve both short and long-term adjustment of children identified as being "at risk" for conduct disorder. Classes were conducted in 32 elementary schools in a group format for boys, 9-10 years of age.

Conduct disorder in children is clinically defined as a constellation of problematic, non-compliant, defiant and oppositional behaviors in which the basic rights of others or age appropriate norms are violated, and that are repetitive and persistent (lasting at least 6 months). It is also referred to by such labels as antisocial, aggressive, acting out, and externalizing behaviors of children and adolescents. From a societal perspective, children who exhibit these behaviors often are identified as delinquents.

It is estimated that up to 10 percent of boys 7-10 years of age exhibit this disorder. Conduct Disorder is most prevalent in inner city areas, is three times more prevalent in boys as girls and is the most frequent reason for referral of children to outpatient mental health services.

The causes of conduct disorder are not well understood. Although there is some evidence of a genetic component for the expression of aggressive behavior, most of the etiological research has focused on community influences, parent deviance, parent management skills, coercive family interactions, and peer rejection. Recent work also emphasized the importance of social cognition in the development of conduct disorder. Poor academic performance also has been correlated with conduct problems.

Given this information about the epidemiology, etiology and pathogenesis of conduct disorder, researchers have developed several interventions for preventing its onset and development. In general, these interventions have focused on altering the response repertoire of high risk, inner city children by fostering behaviors such as cooperation and other positive social skills that are inconsistent with problem behaviors. Some interventions also attempt to change the cognitive processes underlying social behaviors (e.g., by fostering alternative thinking). Another strategy has been to foster verbal and other academic skills so as to reduce acting out in the classroom associated with poor academic performance. Parent management training has also been used as an intervention for conduct disorder.

NIMH currently supports four AIDS research centers, three of which are in cities with a high prevalence of AIDS cases and HIV infection (New York, Miami, and San Francisco). Each center has a major focus on minority populations.

The HIV Center for Clinical and Behavioral Studies at Columbia University, New York, has ongoing prevention projects in schools and with high risk populations of adolescent runaways. Many subjects in these studies are inner-city minority adolescents. This center is also conducting studies in minority populations on behavioral manifestations of HIV infection, disease transmission and progression, and prevention of HIV infection. The Center for the Biopsychosocial Study of AIDS at the University of Miami is conducting prevention projects in Hispanic and Haitian populations. The Miami Center is investigating psychosocial, immunologic, and neuropsychological aspects of the spectrum of HIV infection in a wide range of at-risk populations, including several minority populations. These centers are also investigating neurodevelopmental and cognitive deficits in babies with HIV infection, a population which is composed almost exclusively of minority children.

The Center for AIDS Prevention Studies, University of California at San Francisco, has a component entitled Multicultural Inquiry and Research in AIDS Area which conducts behavioral research and prevention projects in minority communities.

RESEARCH TRAINING

The goal of NIMH research training programs is to support initial training opportunities and career development of the leaders in the next generation of the Nation's mental health researchers. The specific objective of the programs concentrating on minority trainees is to ensure that they have a prominent leadership role, with outstanding training and a full range of research opportunities.

One of the most significant research training programs is the ADAMHA Minority Access to Research Careers (MARC) program for honors undergraduates and for faculty fellowships. These awards, made to institutions with substantial minority enrollments, provide support for high-level research experiences for promising junior and senior level college students working closely with a faculty sponsor. Support is also provided for selected faculty members to undertake more specialized research fellowships. Awards were recently made to support three new MARC programs - University of Puerto Rico at Rio Piedras, University of New Mexico and the University of Hawaii at Manoa. A total of 13 institutions now participate in this effort. Support is targeted to assist qualification for entrance into doctoral level or M.D. programs in disciplines related to alcoholism, drug abuse, and mental health. This approach further strengthens Institute efforts directed at recruiting and training minority individuals.

Support for research training is also available to graduate students in key disciplines through the Minority Fellowship Program (MFP). Research training awards are made to national professional associations in psychiatry, psychology, sociology, nursing and

social work. MFP directors and selection committees at the respective association, in turn, recruit, select, and closely monitor highly qualified graduate students in accredited doctoral programs throughout the country. In addition to providing stipend support, personal support and network opportunities are provided. The most recent addition to the program, Psychiatry, was designed to support the development and training of psychiatrists to undertake active, productive careers in scientific investigations related to mental health and mental illness.

To further enrich and strengthen the research environment of minority institutions, a new program entitled Minority Institution Research Development (MIRDP) Program has been initiated. This effort provides grant support to develop and/or expand existing institutional capacity for conducting mental health research and to enhance the research capability of faculty to conduct neuroscience, behavioral, biological and social science research in mental health. Undergraduate and graduate minority students will benefit directly from participation in research projects as research assistants, and will be encouraged to pursue careers in mental health research.

ALCOHOL, DRUG ABUSE AND MENTAL HEALTH ADMINISTRATION

Office for Treatment Improvement

Minority Health and Assistance

The Office for Treatment Improvement (OTI) provides assistance to minority populations through their categorical grants and the ADMS Block Grants. Because approximately 43% of those in substance abuse treatment programs are minorities, 43% of all OTI funds will be directed to minority populations in FY 1991. The categorical grants (Treatment Improvement Grants and Grants to Crisis Areas) will provide $52.3 million to minority treatment programs. Because of the lack of specific information and the difficulty of estimating the amount of Block Grant funds going to minorities, we have not included estimates in the funding table.

HEALTH RESOURCES AND SERVICES ADMINISTRATION

Bureau of Health Professions

Minority Recruitment Activities

Minority recruitment initiatives were carried out among a number of the Bureau's training and grant programs in response to the national concern that minority groups continue to constitute a relatively small percentage of workforce in most health professions.

Fifteen Area Health Education Center programs indicated efforts aimed at minority recruitment of health professionals. Thirteen of these programs received funds totaling $484,143, which are estimated to affect 34,147 individuals. The University of Massachusetts received $53,891 to support a project that will train minority high school students from medically underserved areas to function as student health educators.

Under the section 786(a) Family Medicine training programs, four predoctoral, four residency, and 13 faculty development grantees reported minority recruitment activities. An estimated 26 residents will benefit from support of this initiative.

Five General Internal Medicine/General Pediatrics Residency program grantees have instituted minority recruitment activities, as have two of the faculty development program grantees.

A total of $549,959 was awarded among 19 of the 36 programs to train Physician Assistants who maintain emphasis on the recruitment and retention of minorities in their programs. An estimated 305 trainees will benefit from these efforts. The largest award was for $142,982 to Howard University. Their entire program is focused on minority training affecting an estimated 39 Physician Assistant trainees.

Three Preventive Medicine Residency Training grantees indicated involvement in minority recruitment for programs which would benefit an estimated 8 individuals.

One of the Two-Year programs of Schools of Medicine and Osteopathy indicated minority recruitment as a part of their program activities. No specific funds were requested for this initiative.

Among the Geriatric Medicine and Dentistry Faculty Training projects supported during FY 1989, 22 will focus on the recruitment and training of minority faculty.

Nine of the Podiatric Primary Care Residency program grantees received a total of $133,799 for their minority recruitment and training initiatives impacting 72 residents.

Minority training was particularly noted as an emphasis of the educational activities carried out by five AIDS Regional Education and Training Centers programs.

Nursing Education Opportunities for Individuals from Disadvantaged Backgrounds

The objectives of this program is to increase nursing opportunities for individuals from disadvantaged backgrounds by identifying, recruiting and selecting such individuals; facilitating their entry into schools of nursing; providing counseling or other services designed to assist such individuals in completing their nursing education; providing, prior to entry into a school of nursing preliminary education designed to assist them to successfully complete such regular course of education; paying such stipends; publicizing financial aid available to persons enrolled in schools of nursing, and faculty development, providing training, information, or advice to the faculty of such schools with respect to encouraging such individuals to complete the programs of nursing education in which the individuals are enrolled.

Excellence in Minority Health Education

The Excellence in Minority Health Education program addresses the disparities in the health status of minorities and their underrepresentation in the health professions. Specifically, it is intended to strengthen the national capacity to train minority students; and to support the health professions schools which have trained a significant number of the Nation's minority health professionals, and enable those schools to supply health professionals to serve minority populations in underserved areas. Such will be achieved through awarding grants to eligible health professions schools for purposes of developing plans to achieve institutional improvements, including financial independence; improving capacities to recruit and retain faculty; student recruitment; student performance; improving access to information resources; and developing curricula and faculty in order that the school become a resource with respect to the health problems of minority communities, such as higher infant mortality rates and higher incidence of acquired immunodeficiency syndrome.

This program serves as the principal Federal activity supporting certain predominantly minority institutions which train a disproportionate number of minority health professionals as well as provide a great deal of care to minority populations. These schools are recognized for their special capacity to conduct activities to prepare health professionals to serve minority populations.

Health Careers Opportunity Program (HCOP)

The Health Careers Opportunity Program's long-range goal is to promote a nationally equitable health delivery system by increasing the access to health careers and services for individuals from disadvantaged backgrounds. The specific objective of the Disadvantaged Assistance Program is to provide a National focal point and to assure that the health resources required to meet the health care needs of disadvantaged Americans are comprehensively addressed. The program increases the number of individuals from disadvantaged backgrounds entering into and successfully completing a health or allied health education. This program also addresses the imbalance of minority health professionals and helps correct the disparity of health care services available to minority communities.

Achieving the long-range goal is made possible by awarding grants and contracts to health professions schools and other health or educational entities to assist individuals from disadvantaged backgrounds to undertake and complete education in health professions, public health and allied health professions, and through projects designed to identify, motivate, recruit and provide preliminary and enrichment education to disadvantaged individuals in order to facilitate their entry into and graduation from such schools.

This program serves as the principal Federal health training activity for underrepresented minorities and other students who are financially or otherwise disadvantaged. Operationally, the program focuses on educational institutions by requiring 70 percent of the funds be awarded to institutions of higher education, 10 percent be obligated to community based programs, and not more than 5 percent of such funds may be awarded for projects whose primary purpose is informing individuals about the existence and general nature of health careers. From 1972 through 1987, approximately 68,525 trainees formally participated in structured programs designed to provide them the skills, educational background, or enrichment help necessary to facilitate their entry into and/or retention in health professions schools. Thousands of others benefitted from general counseling, motivation, tutorial and recruitment efforts, and were provided special aid and other information concerning health careers. Studies by the Division of Disadvantaged Assistance show that students from HCOP-supported undergraduate schools have higher admission rates to medical schools than students from non-HCOP undergraduate schools when grade point averages and Medical College Admissions Test scores are equivalent. The studies also show that the graduation rate for minority students in medical schools with HCOP retention programs is higher than for like students in medical schools not having HCOP retention programs.

Financial Assistance for Disadvantaged Health Professions Students

Authorizing legislation directs that, of the total funds appropriated for Disadvantaged Assistance, 20 percent shall be made available for stipend support for financial assistance for disadvantaged health professions students who are enrolled in a school of medicine, osteopathy, or dentistry.

Exceptional Financial Need Scholarships

The Exceptional Financial Need Scholarship program assists persons with limited resources to attend one of the health professions schools (medicine, osteopathy, dentistry, veterinary medicine, optometry, podiatry, and pharmacy). These scholarships assist full-time students with exceptional financial need. Funds are allocated to participating health professions schools which in turn are responsible for selecting the students to receive the scholarships. Priority is given to schools of allopathic and osteopathic medicine and dentistry. Recipients may receive monthly stipends for living expenses, plus tuition and other reasonable education expenses, without incurring a service obligation.

H.P. Institutional Development

In FY 1991, $12,000,000 is requested to support a new Health Professions Institutional Development program which will assist schools with a majority of minority students, to develop improved faculty training (Faculty Development Component) and to provide limited funding flexibility for institutional improvement (Academic Reinforcement/Institutional Improvement Component) without risking further erosion of their financial status.

Community Based Recruitment and Support

In FY 1991, $5,000,000 is requested for a new Community Based Recruitment and Support program that provides grants to support innovative community-based efforts to recruit potential health professions students from the community and support their health professions training.

In addition to providing financial assistance, the Department would provide technical assistance in establishing contracts between the communities and the health professions students regarding the service obligation as a health professional in the local community.

Health Resources and Services Administration
Health Care Delivery and Assistance

This new program supports loan repayments and special scholarships to financially disadvantaged health professions students for the purpose of increasing the recruitment of such students to serve in the community with which they are familiar. this new initiative will allow the student more flexibility in fulfilling the service obligation. It is based on the premise that individuals may be more likely to enter health professions training if they know they can obtain financial assistance in exchange for providing health services in communities with which they are more familiar, even if the period of the service obligation were longer than what is normally required of National Health Service Corp obligors.

HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Health Professions

Native American Indian Activities

Seven of the Bureau's grant programs received a total of $669,738 for education and training efforts specifically related to the health care of the Native American Indian population.

Seven of the Area Health Education Center (AHEC) grantees indicated a commitment to training in this area and received awards totaling $541,377 estimated to affect 157,000 trainees and population. The largest award ($315,110) was to the University of Washington (WAMI) AHEC for their recruitment and training initiatives focusing on the Alaska Natives and Native American population in that region.

Four section 786(a) Family Medicine Predoctoral training program grantees reported specific activity to benefit the Native American population.

One of the section 784 General Internal Medicine/General Pediatrics Residency training programs indicated that their training would include some exposure of the residents to the health care needs of the Native American Indian population.

Sixteen grantees indicated that their Physician Assistant Training programs would expose 23 students to the health care of Native American Indians, using such training modalities as clinical rotations on Indian reservations. A total of $52,536 was requested by grantees for program initiatives in this area.

The Two-Year Training program at the University of Minnesota will focus on recruitment and training of Native Americans. An estimated 48 students will benefit from these initiatives for which $75,825 was specifically requested.

Two AIDS Regional Education and Training Center projects will focus on HIV/AIDS issues relevant to the Native American population.

HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Health Professions

Hispanic Initiative

In 1985, Hispanic Americans were estimated to be 7.2% of the Nation's population. Many of them reside in rural areas or urban ghettos which are generally classified as medically underserved. It is interesting to note that despite the dramatic increase of Hispanics in this country, the ratio of health professionals to this population remains disproportionately low. Medical school entrants include only 4.2% Hispanic students, further frustrating the problem of training health professionals who are sensitive to the health and cultural needs of this population. The Bureau continues to fund through its grant programs, efforts to recruit and train Hispanic health professionals.

I. Area Health Education Center (AHEC) Program (section 781)

It is not unusual that in those States which have a large Hispanic population as well as an AHEC program, efforts to recruit and train Hispanics for the health professions are significant. An estimated $618,350 was spent by the 6 AHEC projects which specifically indicated efforts affecting over 383,950 individuals. The College of Osteopathic Medicine of the Pacific received $195,000 for its targeted multicultural AHEC program activities reaching approximately 2,500 individuals. The California Hismet program is a vehicle by which new and expanded recruitment and teaching programs are developed to increase the numbers of Hispanics in the health professions and improve access to health care for that population. Under this program, a new Hispanic residency program in Family Medicine is being established.

The University of Arizona received $400,000 for its work along the border of Mexico to train health professionals who will develop services for Mexican Americans living in urban ghettos as well as the agricultural areas of Arizona. All of the projects are particularly targeted to develop medical clerkships and residency programs as components of their programs.

II. Family Medicine Training (section 786(a))

Six grantees under the residency program reported activities targeted for Hispanics in which 33 trainees will participate.

The University of Puerto Rico concentrates on training Hispanic individuals as part of its Section 780 Family Medicine Departments grant activities.

III. Physician Assistant Training Program (section 783)

Twelve Physician Assistant Training program grantees reported activities which specifically benefit the Hispanic population (either through recruitment or curricular/clinical activities). An estimated 74 trainees will be affected. No specific funds were requested for these activities.

IV. AIDS Regional Education and Training Centers Program (section 301)

Five grantees indicated a Hispanic initiative in their training program activities. No specific funds were requested for this area of emphasis.

CENTERS FOR DISEASE CONTROL

SEXUALLY TRANSMITTED DISEASE
Minority Health

A major objective of the Division of Sexually Transmitted Disease is to develop effective and culturally relevant programs to inform and educate the general public, particularly members of minority populations, to gain broad support and acceptance of STD prevention program efforts throughout the U.S. and its territories.

Although not specifically targetted to minorities, project grants awarded to State and local health departments and appropriate public and nonprofit entities emphasize the reduction of morbidity and mortality from STD, particularly in minority inner-city, heterosexual populations - the same groups that are at high risk of HIV infection associated with IV drug abuse.

In FY 1989, STD prevention and control activities for minority populations included the involvement, through grants to states and direct funding, of almost 400 Community Based Organizations who represent and serve culturally diverse populations.

Tuberculosis
Minority Health

The burden of tuberculosis is being increasingly borne by racial and ethnic minority populations. During 1988, over 65 percent of all tuberculosis cases occurred among racial and ethnic minorities. Relative to the incidence rate of 4.1 per 100,000 in non-Hispanic whites in 1988, the relative risk of developing tuberculosis in Asians was 9-fold higher; in non-Hispanic blacks, 7-fold higher; in Native Americans, 4-fold higher, and in hispanics, 4-fold higher.

Although not specifically targeted to minorities, cooperative agreements awarded to State and local health departments emphasize the reduction of morbidity and mortality from TB in high-risk groups, particularly in racial and ethnic minority populations.

Immunization
Minority Health

The Division of Immunization does not presently collect specific data on minority health students and schools. However, the delivery system of the public health agencies is primarily focused toward that population that would be considered less able to afford the services of the private medical system. The immunization status of children entering the nation's school systems is at an all time high, with 98 percent of the children in the kindergarten/first grade vaccinated against measles, rubella and mumps and 97 percent of these children have received 3 or more doses of polio and DTP/Td/DT.

There are a few pockets of low immunization levels in the preschool population residing in the low income, urbanized areas of the Nation: these levels may be as low as 50 percent. The overall immunization level in the preschool population is estimated to be 75 percent to 80 percent.

During FY89 the Division of Immunization is conducting, through an outside vendor, an assessment of immunization status in a low income, urbanized area, with the purpose of developing a model that can be used in future assessments of similar areas. The assessment is scheduled for completion in September, 1990.

In 1990, Congress appropriated $7,881,000 to develop successful approaches for raising the age-appropriate immunization levels of our nation's children, particularly the hard-to-reach populations in large, inner city areas.

INFECTIOUS DISEASES/HEPATITIS B
MINORITY HEALTH

Hepatitis B has a disproportionately high incidence among blacks, Hispanics, Pacific Islanders, Alaskan Natives, Asian-Americans and Asian immigrants. Defining the risk of HBV infection in various minority groups has been approached in several ways. The Sentinel County Study of Viral Hepatitis and the Viral Hepatitis Surveillance Program (VHSP) provide information on the incidence of infection and risk factors associated with infection among ethnic groups. The prevalence of HBV infection has been defined from serologic studies of the National Health and Nutrition Examination Survey (NHANES II), Hispanic HANES and in other special epidemiologic studies of Asian populations.

A vaccine demonstration project and a statewide Alaskan Native vaccination program initiated in 1981 and 1983, respectively, have markedly reduced the annual incidence of disease among Alaskan Natives. Persons vaccinated in 1981 are being followed annually to identify new infections and measure antibody levels, and thus determine the need (if any) for a booster dose of hepatitis B vaccine. Immunogenicity studies utilizing various vaccines, dosage amounts, and schedules are planned. Hepatitis B surface antigen carriers are being followed and tested annually with alpha-fetoprotein (AFP) to detect early, resectable liver cancers. A vaccine demonstration project in American Samoa (1985) established the screening of pregnant women for HBsAg and the treatment of their infants, provided HB vaccine for all susceptible persons in the population, and integrated HB vaccination into the routine childhood immunization program. In other Pacific Islands affiliated with the U.S. (Guam, Saipan, Palau, Micronesia), hepatitis B immunization programs have been initiated (1988) through the cooperative efforts of the local public health departments, the Department of Interior, local Maternal and Child Health Programs, and the US Public Health Service (Region IX and CDC).

In 1988, the Immunization Practices Advisory Committee (ACIP) recommended that all pregnant women in the U.S. be screened for HBsAg to prevent mother-to-infant transmission of HBV. Of the estimated 18,000 pregnant women who are found to be HBsAg positive each year, 48% are Asian, 19% are black and 11% are Hispanic. Beginning in FY 1990, resources will be available to states to supplement programs designed to screen pregnant women for HBsAg, provide HB vaccine and HGIG to their infants, and screen and vaccinate susceptible household contacts.

Also occurring in particularly high incidence among Alaskan Natives are meningitis, pneumonia, septicemia, and other diseases due to invasive H. influenzae and S. pneumoniae. A statewide laboratory-based surveillance of all isolates of these organisms from sterile sites (blood, spinal fluid, etc.) is ongoing. Data from surveillance include confirmation, serotyping and antibiotic sensitivity testing. A program is currently underway in cooperation with one Native regional health corporation to assure vaccination of all persons at high risk for pneumococcal disease and enhance blood culturing practices in the region. To reduce H. influenzae disease in Alaskan Native children, BPIG (bacterial polysacharide immune globulin) is being administered to all infants in one service unit. In another area, the four available H. flu-conjugate vaccines are being evaluated in immunogenicity trials.

In addition, invasive cervical cancer is diagnosed in Alaskan Native women at more than twice the rate of that of the U.S. white population. Studies are underway to determine the overall prevalence of infection of human papilloma virus (HPV) infection and the specific types of infection in women with cancer, those referred to colposcopy clinics, and women undergoing routine Pap smear. A case control project is also ongoing to determine risk factors for cervical neoplasia.

Other infectious diseases of particular significance to minority populations include plague, dengue, sickle cell anemia, and Human Parvovirus B19 infections. Plague is an acute bacterial infection spread to humans by wild rodents and their fleas. The disease occurs most commonly in Hispanic and native American populations in Arizona and New Mexico. The major efforts to contain this disease include active surveillance and development of educational programs targeted to Hispanic populations and native American tribes in the southwestern United States. Epidemic dengue and dengue hemorrhagic fever, transmitted by the Aedes Aegypti mosquito, are a major disease problem in Puerto Rico and throughout the Caribbean Basin. Ongoing programs for prevention and control of dengue include surveillance, mosquito containment initiatives, and widespread community education programs. Sickle cell anemia and human parvovirus B19 infections occur predominantly in blacks and Orientals. CDC involvement includes outbreak investigation and epidemiologic studies.

CHILDHOOD LEAD POISONING PREVENTION

MINORITY HEALTH

Lead is ubiquitous in the environment; adults and children are exposed to it from many sources--air, water, food, dust, soil, and paint. Young children, especially those from birth to five years of age, are much more susceptible to available lead than are adults. Childhood lead toxicity is prevalent in many communities, large and small, located in all sections of the country. For example, the "Second National Health and Nutrition Examination Survey, 1976-1980" conducted by the National Center for Health Statistics to measure blood lead levels in the general United States population, found that four percent of all children from six months to five years old had blood lead levels of at least 30 micrograms per 100 ml of blood (ug/dl). The percentage of children with these elevated lead levels ranged from 2.1 percent in rural areas to 11.6 percent in inner cities.

In young children, excessive lead exposure can produce injury to the hematopoietic (blood-forming), renal (kidney), and nervous systems. Damage to the nervous systems ranges from severe mental retardation to subtle intellectual deficits, behavioral disorders, and learning disabilities. These latter consequences have received greater recognition by the general medical community since 1980. In particular, these impairments result from levels of lead exposure previously considered safe, and occur in children who are otherwise asymptomatic.

An estimated 3-4 million children have high enough levels of lead in their blood to cause adverse health effects. The problem is particularly serious and widespread among minority, poor, and inner city children. It has been estimated that nearly 70 percent of poor, inner city black children six months through five years old have high enough blood lead levels to cause adverse health effects.

CDC continues to work to identify sources of lead in the environment which may be particularly dangerous to children. In cooperation with State health departments and the Environmental Protection Agency (EPA), studies (in Kellogg, ID, and East Helena, MT) were conducted to measure sources of environmental lead in children and their homes and yards. The Kellogg study has led EPA to plan remedial actions for high soil lead contamination. In 1987, CDC began providing consultation to EPA in selecting sites and designing studies for demonstration projects to remove leaded soil in metropolitan areas. Currently, CDC has an interagency agreement with EPA to provide scientific and logistic support for a three-city study of leaded soil abatement.

In cooperation with the Health Resources and Services Administration (HRSA), CDC has continued to operate the Blood Lead and Erythrocyte Protoporphyrin Proficiency Testing Programs to provide quality assurances to nearly 300 participant laboratories.

The Congress, recognizing that an expanded strategy needed to be developed to eliminate the childhood lead poisoning problem, recently passed legislation that will provide grant funds in Fiscal Year 1990, administered by the Centers for Disease Control, for intensive community lead screening, follow-up, and community education and outreach programs. State health agencies are expected to play a key role in the development of these community-based childhood lead prevention programs.

In Fiscal Year 1990, CDC is planning for the development of a childhood lead poisoning prevention grant program; providing technical assistance and consultation to State and local governmental agencies, other Federal agencies, academic and research institutions, interests groups, and others on issues of lead exposure and poisoning; revising the CDC statement Preventing Lead Poisoning in Young Children; continuing to provide proficiency testing and reference laboratory services; and conducting epidemiologic studies on the relationship between exposure to environmental lead and blood lead levels.

MINORITY POPULATIONS

MINORITY HEALTH

Projects were implemented for the prevention of disabilities including developmental disabilities, injury disabilities from head and spinal cord trauma, and secondary disabilities. Surveillance activities and planned community programs for the prevention of primary and secondary disabilities will assess the disproportionate incidence and prevalence for specific disabilities among minority populations and the poor, and will give attention to the design of community-based prevention interventions to address those issues.

Surveillance, epidemiologic studies, and interventions for birth defects (including fetal alcohol syndrome) and developmental disabilities (including mental retardation) are being continued, as well as studies of potential environmental causes of low birth weight. These efforts are being conducted in a multiracial population that includes a large portion of blacks.

The Medical Examiner/Coroner Information Sharing Program, a surveillance system based on medical examiner/coroner (MEC) cases, involves a nationwide network of MECs to collect uniform and timely data on unanticipated deaths (such as homicides, suicides, unintentional injuries, acute poisonings, sudden infant death syndrome, deaths from disasters, and drug overdoses), and seeks to develop better ways of sharing information among MECs, the public health community, and other interested groups, especially minorities.

The Centers for Disease Control (CDC) natural disaster emergency response plans were thoroughly tested with the occurrence of hurricane Hugo, which devastated St. Croix in the Virgin Islands and severely damaged parts of Puerto Rico and North and South Carolina; and an earthquake which destroyed bridges, highways, and buildings in the San Francisco Bay area. These two disasters resulted in considerable morbidity and mortality among minority populations, and we are hopeful that the epidemiologic studies being conducted will yield useful information to help minimize similar outcomes in the future.

CDC provides external quality assurance for neonatal screening for congenital hypothyroidism, phenylketonuria, and galactosemia. Planning is underway to add sickle cell disease, which is a significant disease in blacks. CDC has a major program in improving the laboratory measurement of cholesterol and other lipids which are important in diagnosing and treating cardiovascular disease. This program is of particular importance to blacks because cardiovascular disease is more prevalent in that population than in the white population.

In the Third National Health and Nutrition Examination Survey (NHANES III, 1988-1994), CDC is characterizing the exposure of the general U.S. population to lead and cadmium. Lead exposure is higher in blacks than other races. This survey will identify the extent of current lead exposure in whites, blacks, and Hispanics, and determine groups that should be special targets of prevention efforts. Also, in NHANES III, measurements are being made which characterize the nutritional status of whites, blacks, and Hispanics.

The Center for Environmental Health and Injury Control is responsible for reducing injury related morbidity, mortality, disability, and cost. The burden of injury rests disproportionately among the poor--many of whom belong to minority groups. The DHHS report on minority health identified injury as one of six problem areas that cause "excess deaths" - that is, the difference between the number of deaths observed among blacks and the number of deaths that would have occurred if blacks died at the same rate, for each age and sex, as whites.

In 1984, blacks represented 12% of the population but accounted for 15.3% of all deaths due to injury. The four causes of injuries with the largest disparities in black-white deaths in that year were homicides, residential fires, drownings, and pedestrian mishaps. Homicides accounted for the greatest disparity in injury mortality rates between blacks and whites.

- Homicide is the leading cause of death for black males 15-34 years of age and will be the cause of death for 1 black male in 28.
- The homicide rate for blacks was 29.0 per 100,000, which is 5 times that for whites (5.5 per 100,000).
- For both males and females, homicide rates were highest among young adults ages 20-39.
- Rates were higher for black males than any other race-sex group.
- Black males had almost twice the fire death rate of black females, and over 3 times the rate of white males, and over 5 times the rate of white females.
- Black males had twice the death rate from drowning of white males, over 7 times the rate of black females, and over 8 times the rate of white females.
- Black males had nearly twice the death rate from pedestrian motor vehicle collisions of white males, more than 3 times the death rate of black females, and over 4 times the rate of white females.

In 1986, there were more than 1700 excess deaths of black children compared to white children for the same 4 causes. Homicides accounted for almost 60% of these 1700 excess deaths.

- Residential fire rates for black children are 3 times those for whites.

Because many kinds of injuries disproportionately affect minorities, most of the activities that CDC carries out to address the injury problem benefit minorities. Brief descriptions of the projects that most significantly benefit minorities are listed below. These projects, however, are not solely targeted to minorities

Injury Prevention Research Centers

- The Southern California Injury Prevention Research Center (SCIPRC) is focusing on the problem of injuries in targeted high risk populations. The SCIPRC is studying intentional and unintentional injuries in ethnic/racial minorities, socioeconomically disadvantaged and other under-served populations in Southern California. Specific aims will include interdisciplinary research on injury causes, prevention, and control in ethnic minority, disadvantaged, or under-served populations.

Research and Demonstration Projects

- The Oklahoma State Department of Health is conducting surveillance of spinal cord, drowning/near drowning, and severe burn injuries. Information will also be collected to elucidate the chain of causation, leading to the development of specific interventions.

- The University of Tennessee is conducting a population based, case-control study to assess the strength and direction of any association between firearm ownership and the risk of violent death in the home.

State Capacity and Surveillance Grants

- The Maryland State Health Department is assisting Baltimore in developing a violence prevention and surveillance system for non-white males (15-34 years of age). Firearms are the leading cause of death for this target group.

- The Minnesota Department of Health is conducting a Positive Parenting Intervention to assess and propose interventions for families at high risk for child maltreatment, targeted in part to blacks and native Americans where homicide rates are elevated.

- The Missouri Department of Health is creating an injury control unit within the Division of Health Resources. Intervention activities will address black homicides, poisoning, and head and spinal cord injuries.

- The New York City Health Department is focusing on Minority Populations in the Central Harlem area. Intervention activities are addressing pedestrian and intentional injuries.

- The North Carolina Department of Human Resources is expanding the capacity of the Division of Health Services to address the problems of intentional and unintentional injuries with particular emphasis on high risk populations and injury prevention strategies in a rural setting.

- The San Antonio Metropolitan Health District will preform "appropriate interventions" in Hispanic and non-white populations, targeting homicide.

- The Washington State Department of Social and Health Services is placing prevention priorities on motor vehicle crashes, suicide, falls, drownings and poisoning among the elderly, children and the poor.

Incentive Grants

- The Kansas City Health Department is working with an inner-city community based anti-crime organization, the Ad Hoc Group Against Crime, to establish an interpersonal violence reduction project in cooperation with the Kansas City Human Relations and Police Departments. The Group will identify high-risk youth and adults who have been involved in violent disputes to supplement actions taken by other agencies (e.g. mediation, probation, suspension, etc.). With conflict resolution, skills (which includes anger control and problem solving) will be targeted toward the groups identified in homicide males between the ages of 17 and 29 who have a prior history of arrest for interpersonal violence and/or weapons charges. Referrals will be accepted from schools, youth serving agencies, police, the juvenile justice system, parents and courts. In addition, outreach workers will make additional referrals, contact adult subjects and parents of troubled youth to obtain their cooperation, and follow up at regular intervals to monitor results. This approach will be supplemented by mass media public education in minority oriented radio and TV programs to teach conflict resolution skills. The project will be evaluated by comparing number of arrests and emergency room contacts for assault injuries for the group participating in the intervention with a control group of residents in similar high risk zones.

- The Philadelphia Injury Prevention Program is developing a model of a feasible injury prevention program that can be implemented in urban areas. The Safe Block Project is a community-based controlled trial that includes block-wide home inspections, modifications and home educational activities.

- The New Mexico Health and Environment Department is evaluating the effectiveness of sobriety checkpoints at selected locations in New Mexico. The final outcome will be a reduction of fatal and serious injuries resulting from motor vehicle crashes.

Other Projects

- In 1985, Detroit had the highest homicide rate of any U.S. city. In 1986, the Detroit City Council passed an ordinance requiring a mandatory sentence for transporting firearms in vehicles and carrying firearms in public. The Detroit Department of Health requested assistance in analyzing the problem of homicide in Detroit and establishing a surveillance system to monitor the impact of the ordinance on the rate and characteristics of intentional injuries.

- Physical violence between individuals who are related, who share the same household, or who are intimate with each other, is increasingly acknowledged as a serious social and health problem. Little is known about the characteristics of perpetrators, the victims, their families and their patterns of involvement with health, social, and criminal justice agencies. The project in Atlanta, Georgia, is a retrospective study of records to examine fatal and nonfatal assaultive injuries among family members and intimates. The project is designed to describe previous agency contacts and make recommendations for providing services related to family and intimate assaults.

- Firearm injury is a serious public health problem. In 1986, 33,400 persons died as a result of firearm injuries. Firearm mortality rates for females, male teenagers, and young adults have been higher during the 1980's than at any time previously. The objective of this project is to determine the feasibility of using the National Electronic Injury Surveillance System (NEISS) of the U.S. Consumer Product Safety Commission to obtain information on the magnitude, characteristics, and costs of the morbidity and disability caused by firearms and on the types of firearms that inflict these injuries.

- The Indian Health Service (IHS) Interagency Agreement with CDC is an effort to develop, implement, and evaluate injury control demonstration projects. Central to this agreement is the Model Community Injury Control Project designed to establish model injury surveillance and injury control programs in three IHS Service Units: Cherokee, North Carolina; Rosebud, South Dakota; and Sells, Arizona.

- Mapping is a useful tool for identifying counties and regions of the country with high rates of injuries. The purpose of this project is to provide a visualization of geographic patterns of deaths associated with selected intentional and unintentional injuries using county-level color maps of the United States. Mapping of rates (per 100,000 population) will consider differences by age, race, and sex. The atlas will also provide age-specific rates of injuries by race (white and other) and sex, and age-adjusted rates by year of death, race, and sex.

- In May of 1988, the Los Angeles Police Department, contacted CDC about an increase in the numbers of youth homicides, particularly in the South-Central region of Los Angeles. From 1986 and 1987, homicides involving victims 10 to 19 years of age increased by 39% in the four county health districts serving this part of the city. In 1987, there were 32 homicides in Los Angeles involving victims less than 18 years of age which were classified as gang homicides. Through October of 1988, there have been 36 such homicides.

- The Miami Falls Study will determine the epidemiologic characteristics of elderly falls, environmental and host risk factors associated with falls, possible control measures, and the effectiveness of control measures in reducing morbidity, mortality, and medical costs. The surveillance phase, begun in June 1985, includes all falls reported by hospitals, the ambulance service and the medical examiner, among persons 65 and over in four-census tracts of South Miami Beach, Dade County, Florida. The case-control study begun in January 1987, is comparing 600 surveillance cases with 800 population-based controls.

Several important CDC-related efforts lend strength to the overall outreach to minorities. In its second meeting, the Advisory Committee on Injury Prevention and Control recommended that there be increased attention to intentional injuries which have a disproportionate impact on minorities. Likewise, in developing the Year 2000 Objectives greater emphasis has been placed on controlling violent and abusive behavior. In addition, a National Academy of Science Panel on Violence is exploring ways of understanding and controlling violence. CDC is supporting an American Medical Association Conference on family violence, a problem which takes a heavy toll on the poor and minorities. CDC also plans to support a conference addressing violence and public health in 1990.

Chronic Disease Prevention/Health Promotion

Minority Health

The disadvantaged and minorities bear a disproportionately large burden of preventable illness and death in this country. Their special needs present an enormous challenge to public health. Aggressive attention to the greater health risks of disadvantaged and minority populations will contribute to the reduction of morbidity and mortality in this population. CDC is targeting these populations through the following activities.

- Monitoring the Nutritional Status of Low-Income, High-Risk Populations

  The Pediatric and Pregnancy Nutrition Surveillance Systems monitor the nutritional status and behavioral risk factors of low-income, high-risk populations of women, infants, and children receiving services in publicly-funded health, nutrition, and food assistance programs. Nutrition surveillance data are used to identify and better target interventions for these high-risk populations.

- Identification of Severely Undernourished Children Missed by Traditional Public Health Care System

  Children from disadvantaged families are at greater nutritional risk. Surveillance for severe undernutrition in children is being implemented in four States. An important feature of the system is a hospital-based component to identify children who may have been missed earlier by the traditional public health care system. Hospitals are the last resort source of health care for many low-income, disadvantaged families as medical care may not be sought until after a child has become seriously ill. Data from the surveillance network will be used in programmatic decisions such as outreach, the early identification of disadvantaged children at risk for severe undernutrition, and improved access to food assistance programs and social services.

- Early Detection of Breast and Cervical Cancer Among Those Underserved

  State-based demonstration projects on breast and cervical cancer are currently identifying barriers to the early detection of breast and cervical cancer in underserved populations. These projects are designing and implementing interventions to accomplish changes to prevent mortality from these cancers in targeted populations, including urban black women, white rural women, and Native American women.

- Reducing the Black/White Gap in Low Birthweight and Infant Mortality

  The Secretary's Task Force on Black and Minority Health issued its report in 1985. CDC played a major role in developing the report's recommendations for reducing the black/white gap in low birthweight and infant mortality, one of the six major areas identified by the Task Force for intervention. Since the inception of the Office of Minority Health, CDC has chaired the Working Group on Infant Mortality. Most of the Task Force recommendations have been implemented and are being tracked.

Specifically:

- The CDC-coordinated National Infant Mortality Surveillance project provided infant mortality data by birthweight for infants born in the U.S. in 1980. Key findings indicated that the most important predictor for infant health survival is birthweight, and the survival rate increases exponentially when birthweight is increased to its optimum level. Over one-half of all deaths of single-delivery infants occur to the 6 percent of live-born infants with low birthweight. Furthermore, regardless of infant and maternal risk factors, black infants have a twofold higher mortality rate than white infants. These findings have promoted new national efforts to reduce low birthweight, examine risk factors for excess black infant mortality among lower-risk mothers, target States at higher risk of infant mortality for intervention, and develop surveillance of Sudden Infant Death Syndrome (SIDS).

- Since 1986, CDC has worked closely with three State health departments to develop and implement programs to assist pregnant women attending public health clinics to quit smoking. Preliminary data indicate that projected quit rates are being exceeded and that 50 percent more women are quitting in clinics that are offering the intervention, as compared to women in clinics that are not. As a result of these successful efforts, CDC is now positioned to take the lead in helping other States deliver smoking cessation interventions to pregnant women.

o Involvement of Minority Communities in Health Promotion Programs

Health promotion activities among minorities and minority communities are being emphasized. For example, at least 50 percent of intervention efforts developed and implemented through CDC's Community Chronic Disease Prevention Program are being targed toward high-risk, minority populations. Protocols for interventions incorporate community organization techniques tailored to minority communities. Increased attention is being given to the importance of the community's infrastructure and leadership and to the inclusion of a broad array of organizations in developing intervention protocols. Similarly, family values and the role of churches have also been emphasized.

o Strategies to Combat Smoking Among Minorities

The Roundtable on Smoking and Minorities was formed as a result of a meeting of the Interagency Committee on Smoking and Health to address the health of minorities. The Roundtable focuses on strategies to combat smoking among minorities. Participants include the Office on Smoking and Health; the American Cancer Society; the American Heart Association; the American Lung Association; the Association of Minority Health Professions Schools; the Office of Minority Health; the National Cancer Institute; and the National Heart, Lung, and Blood Institute. The CDC's Office on Smoking and Health has conducted a number of analyses of smoking behavior (initiation, current use, and quitting) by race. The Office of Smoking and Health also produces and distributes a series of racially-sensitive television and radio public service announcements, as well as print materials.

- Reducing Premature Death and Disability from Cardiovascular Disease

Cardiovascular disease resulted in over 760,000 deaths and over 1.5 million years of potential life lost in 1986. To have a widespread impact on reducing cardiovascular disease (as well as other preventable chronic diseases) in the United States, we must replicate lessons learned from several major community trials using community-based approaches to reducing modifiable behaviors that place individuals at increased risk for disease. The South Carolina Cardiovascular Disease Prevention Program is serving as a learning laboratory for identifying successful strategies for implementing community-based interventions. Baseline surveys of the population, a community resource inventory, and several epidemiological studies have been completed. Public awareness events with the local media have promoted targeted intervention activities, including a Get Fit Campaign; television home study course on the USDA nutritional guidelines; blood pressure and blood cholesterol screening; self-help kits for fitness, nutrition, weight control, and smoking cessation; walking trails; and training for health professionals on cholesterol control and smoking cessation. In addition, CDC is assisting Alabama, Maine, California, and Ohio to build their capacities to implement interventions targeted toward health behaviors in selected communities. Heart health training for teachers, inservice education for physicians, and cholesterol screening have been implemented, with half of all intervention efforts directed toward high-risk, minority populations.

Minority Health (HIV)

In fiscal year 1989, an office on minority health activities (HIV) was established and staffed at CDC to ensure that HIV prevention programs are targeted to minority populations and that technical assistance is provided in the implementation of those programs.

In fiscal year 1987, CDC began specifically targeting funds to address HIV infection among racial and ethnic populations minority by awarding more than $7 million to 41 State and local health departments to support community-based initiatives to prevent infection among minorities at risk for HIV infection. Approximately $15 million was awarded to 52 State and local health departments for similar initiatives in fiscal year 1989.

In fiscal year 1989, CDC also provided more than $5 million directly to selected community-based minority organizations in 27 metropolitan areas having the largest number of reported AIDS cases.

In addition, CDC awarded cooperative agreements to 20 national organizations to help schools and other agencies serving youth provide effective education about HIV. Of the 20 national organizations funded, four specifically targeted their efforts toward black and Hispanic youth. CDC also provides funds to the Indian Health Service for HIV prevention efforts directed to youth.

In fiscal year 1989, the CDC awarded more than $6 million to 32 national and regional minority organizations to assist in developing special approaches to racial and ethnic minority populations and expanding public information efforts directed towards minorities.

In addition, funds are being provided to the United States Conference of Mayors (USCM) to support HIV information exchange and to expand funding to minority-oriented, community-based organizations (23 in 1989) interested in conducting HIV information programs.

In addition to those efforts which are specifically directed to minority populations, the CDC conducts a multitude of HIV prevention activities which also benefit minorities. For example, Perinatal AIDS Prevention Projects, TB/HIV Control Projects, Health Education/Risk Reduction and Counseling, Testing and Partner Notification Programs address high-risk populations which include minorities. Also, information/education messages directed to the public have minority components which are designed by minority advertising firms through subcontracts.

In fiscal year 1990, additional funds in the amount of $14,300,000 will be used to expand the CDC's comprehensive program to prevent HIV infection among minorities who may be at risk. Direct assistance will continue to be provided to minority organizations in 27 metropolitan areas having the highest incidence of AIDS among minorities. Support will also be provided to 10-15 minority organizations to develop and conduct training for local minority groups involved in HIV prevention activities. Efforts to control sexually transmitted diseases (STD) in inner cities will be supported to reduce the risk of HIV infection associated with genital ulcers. Behavioral studies of risk factors and interventions will be conducted.

OFFICE OF THE ASSISTANT DIRECTOR FOR MINORITY HEALTH

The Office of the Assistant Director for Minority Health serves the Centers for Disease Control (CDC) by advising the Centers Director in the determination of the overall CDC policy and planning on minority health; provides leadership in assisting CDC's Centers, Institutes, and Program Offices (CIO's) in identifying minority health problems and issues, and defining appropriate interventions; develops and enhances external contacts regarding minority health issues; coordinates and provides leadership for CDC's participation in PHS and DHHS minority health programs and activities; and assists CIO's and staff offices with programs and activities that have, or should have, special impact on minority health problems.

OFFICE OF THE ASSISTANT SECRETARY FOR HEALTH

Office of Minority Health

Minority Health

The Secretary's Task Force on Black and Minority Health was established in 1984 to explore and document the historical disparity which exists between the health status of minority Americans and the non-minority population. The findings of the Task Force and its resulting report have given the Department a framework within which to address the complex problems underlying the disparities.

The Task Force Report documented over 60,000 excess deaths each year among Asian/Pacific Islanders, Blacks, Hispanics and Native Americans. Excess deaths are defined as deaths that would not have occurred if the death rate of minorities were the same as the death rate for the non-minority population. The Task Force concluded that 80% of the excess deaths were due to six causes: cancer, cardiovascular disease and stroke, chemical dependency, diabetes, infant mortality and violence. Since the issuance of the report, AIDS has been identified as the seventh contributor to excess deaths.

The Office of Minority Health was created to be the focal point for the implementation and monitoring of the Task Force recommendations and for the formulation and development of policies affecting minority health. The Office works closely with the Public Health Service agencies and other components of the Department in a catalytic, coordinative, advocacy and policy development role to: (1) assure that minority health care needs are a priority in Departmental resource allocation decisions, (2) establish short-term and long-range objectives for Departmental health policies addressing minority populations, (3) develop appropriate monitoring systems to ensure that these objectives are met, (4) encourage cooperative and collaborative efforts among PHS agencies to address specific minority health needs, and (5) encourage and initiate the development and use of innovative approaches for decreasing the gap in health status between minority and non-minority populations.

The need for greater Departmental coordination and elevation of the problems of minority health to a level of strategic importance led to the formation of the DHHS - Wide Minority Health Coordinating Process. This was established as a mechanism to define the short and long-range goals and objectives in the various disease areas which contribute to excess deaths among minorities as well three additional health problem areas with crosscutting implications for minority health: financing of and access to health care, health professions and data. Accomplishments to date include the establishment of nine Health Issues Working Groups which have completed a systematic

NINDS intramural scientists Drs. Dale E. McFarlin and Robert J. Fallis are examining the possibility that CREAE may result from responses to introduced antigens by some of the mouse's own immune system's T-cells. They found that the responding T-cells belong to a subset of T-cells that react to antigens presented by class II molecules. (Other T-cells react to antigens in association with class I molecules.)

It has been postulated that, during the immune system's toxic response to antigens, "innocent bystander" cells may be damaged. However, while they do not rule out this possibility, Drs. McFarlin and Fallis detected no such effect in the CREAE mice. Since both astrocytes (cells found only in the nervous system) and endothelial cells (which line blood vessels of the brain and body) are able, under certain conditions, to carry class II molecules on their surfaces that can present antigens, the investigators speculate that these cells may be the biological targets of the T-cells' toxic response in CREAE. Moreover, they could be the means by which T-cells breech the blood/brain barrier and gain entrance to the central nervous system. If the T-cells are then "recycled" through the body, thereby producing their effects over and over again, it could take relatively few of them to produce significant central nervous system damage. Understanding the function of these class II restricted T-cells, which may play an important role in the development of MS as well as CREAE, could lead to the development of therapies to modulate their autoimmune effects.

Emerging Treatment Concepts: International Conference Results

The principal medications physicians use to treat MS today are steroids possessing anti-inflammatory properties. These include adrenocorticotropic hormone (better known as ACTH), prednisone, prednisolone, methylprednisolone, betamethasone, and dexamethasone. While these drugs can reduce the duration and severity of attacks in some patients, they are associated with numerous adverse side effects and are not recommended for long-term use. As evidence of immune system involvement in the etiology of MS has grown, experimental trials of various new treatments to alter or suppress the immune response have been conducted.

To determine the status of current experimental therapies for MS, an international workshop entitled "Diagnostic and Therapeutic Trials in Multiple Sclerosis: A New Look" was held in Georgia November 10-13, 1988. Partially supported by the NINDS, the conference focused on five areas:

- Results of Recent Clinical Trials--Workshop participants concluded that immunosuppressive agents and techniques such as cyclophosphamide, cyclosporine, and total lymphoid irradiation can positively (if temporarily) affect the

assessment of current agency activities and plans which address minority health issues. The next step will be to finalize individual agency-related goals and objectives which will feed into a minority health strategic plan.

A second example of the Office's coordinative functions is its lead role in the Secretary's initiative on health promotion for disadvantaged groups. The Office Director chairs this task force which has been charged with the responsbility for developing an action plan to "improve the health status of minority and low income families and reduce disparities in incidence of premature death, chronic disease and injury received by these families."

Among other ongoing program efforts, the Minority Community Health Coalition Grant Program provides two-year demonstration funding to support community-based organizations which will target risk factor reduction efforts to specific minority groups. These projects are based on the concept that greater force for change can be achieved by expanding the base of awareness, support and involvement. Projects selected for funding have been designed with unique and innovative approaches for the reduction of risk factors for specific health problems in their specific communities. New projects funded in Fiscal Year (FY) 1989 include, e.g., the Continuum Alliance for Healthy Mothers and Children which will address Black infant mortality in Fulton and Terrell counties of Georgia; Community Partnership for the Prevention of Alcohol and Drug Problems Among Latino Youth in Perth Amboy, New Jersey; San Diego Samoan Community Exercise for Better Health Project; and the Fort Defiance Area Native American AIDS Education Project.

The second grant program administered by the Office is the AIDS Education/Prevention Grant Program. This activity as well as other efforts in this health priority area are discussed in the separate program submission for AIDS.

Another accomplishment of the Office of Minority Health is the establishment and operation of the Office of Minority Health Resource Center (OMHRC) which maintains information on minority health-related resources available at the Federal, state and local levels. Components of the OMHRC include a computerized data base of minority health-related materials, organizations, and programs; a nationwide toll-free information line through which OMHRC bilingual (Spanish-English) information specialists respond to inquiries or refer inquiries regarding the seven minority health priority areas to the appropriate organizations and locate relevant materials; and a OMHRC Resource Persons Network which links professionals knowledgeable and active in minority health with minority community-based organizations and voluntary groups who want to become more active in health but lack the technical knowledge to do so.

The Office of Minority Health also sponsors several workshops and conferences throughout each year. Some examples of these are a

National Conference on HIV Infection and AIDS Among Racial and Ethnic Populations, a National Conference on Barriers to Health Care Financing in Minority Populations, and the District of Columbia Violence Intervention Conference: A Matter of Life or Death.

There has in addition, been a continuing demand for technical assistance workshops on grants writing as well as on program specific requirements of the Minority Community Health Coalition Grant Program and the AIDS Prevention/Education Grant Program. The Office also actively supports the Historically Black Colleges and Universities (HBCU) Initiative. Early in FY 1990 the Office conducted two technical assistance workshops specifically for faculty members of HBCUs to improve their ability to compete for Federal financial assistance.

AGENCY FOR HEALTH CARE POLICY AND RESEARCH

Formerly the
National Center for Health Services Research
and Health Care Technology Assessment

MINORITY HEALTH AND ASSISTANCE TO MINORITY HEALTH STUDENTS AND SCHOOLS

The Agency for Health Care Policy and Research (AHCPR) was established on December 19, 1989 as a separate Public Health Service (PHS) agency by the Omnibus Budget Reconciliation Act of 1989, P.L. 101-239. As authorized under a new Title IX of the PHS Act, the purpose of the agency is to enhance the quality, appropriateness, and effectiveness of health care services and to improve access to such services. This goal will be accomplished through the establishment of a broad base of scientific research and through the promotion of improvements in clinical practice and in the organization, financing, and delivery of health care services. The new agency replaces the former National Center for Health Services Research and Health Care Technology Assessment.

As the leader of Federal efforts in outcomes research and health services research, the AHCPR seeks to create and disseminate new knowledge and better understanding of the processes by which health services are made available and how they may be provided more efficiently and effectively. The AHCPR conducts and supports scientific research that tests the assumptions on which current health policies and practices are based, assesses the performance of the health care system, and examines alternate ways to organize, finance, and deliver health services. AHCPR's program is directed towards the needs of health care policymakers, providers, and consumers. It addresses the full array of health care issues, among them minority health care.

Informed policy measures require a systematic analysis of the complex interactions of forces that affect the level and quality of access, utilization, and continuity of health care services for the disadvantaged. Alternative and practical solutions to deal with the specific health care problems of the disadvantaged necessitate an active concern for assessing their relative cost-effectiveness, efficacy, and equity.

For purposes of health services research, the definition of disadvantaged may be considered in terms of income, existing health status and the usual socio-economic covariates that imply a relatively lower class existence in the United States. The likelihood of being faced with inequities in access to health services is magnified if the individual involved is not only poor but also elderly and female, living in a rural or inner-city community, and either Black, Native American, Asian-American, or Spanish-surnamed. However, the definition of the disadvantaged can be broadened as not simply a function of income alone, but as

depending on the number and kinds of access barriers that are faced, the number of special health problems possessed, and the particular personal, social, and economic characteristics of the individuals involved.

Future health services research in this area must be more policy oriented and provide information and appropriate instruments for policy decision-making and program evaluation. Attention will be directed toward analyzing systematically the interaction of the socio-economic, demographic, environmental, and institutional influences that affect health care delivery to the disadvantaged, and identifying the related policy implications and options for various levels of government. Research efforts in this area will address:

- Barriers to access, utilization, and continuity and their modification;
- Determinants of differential morbidity and mortality;
- Institutional and programmatic influences on delivery and use of health services; and
- Cost-benefit and cost-effectiveness analysis of Federal, State, and local programs.

Technical Assistance to HBCUs

Staff of the Agency for Health Care Policy and Research (AHCPR) have served on the training faculties of regional technical assistance workshops sponsored by the Office of Minority Health to train representatives from historically Black colleges and universities (HBCUs) to prepare health services research and clinical research grant applications. In addition, to further involve HBCUs in health services and outcomes research, the Agency will be working with the Health Resources and Services Administration (HRSA) to provide support for their Centers for Excellence.

Extramural Research

The Agency's extramural research program has a multi-faceted approach to minority health care concerns. The centerpiece of this program is the support of research, through peer-reviewed grants and contracts. In addition, the extramural research program provides technical assistance and policy analysis, facilitates timely dissemination of research findings, and works collaboratively with all concerned to assure that activities are coordinated.

Projects Ongoing in Fiscal Year 1989:

"Mediators of Birth Outcomes Among Three Low-Income Ethnic Groups"
Ruth E. Zambrana, University of California at Los Angeles, Grant No. HS05518

Dr. Zambrana is examining the ethnic differences in birth outcomes among primiparous, low-income Black, Mexican-American and Mexican immigrant women who receive their prenatal care from providers in community health centers and primary care centers in public/private hospitals in Los Angeles, California. The study is designed to determine if observed differences in medical risks contribute to differences in birth outcomes, if prenatal care influences neonatal outcomes when medical risk is controlled, if stress and anxiety contribute to birth outcomes, and if the three groups differ in the social support they receive during pregnancy.

New Starts in Fiscal Year 1989:

"Alternative Health Care Utilization in the Rural Elderly"
Dr. James Mitchell, East Carolina University, Grant No. HS05381

Dr. Mitchell will describe and model the use of alternative health care resources by rural poor and black elderly. The variables which influence alternative care use will be identified. Seven hundred and ninety-eight rural poor and black will be identified in 10 of the 33 officially designated rural counties in North Carolina. All respondents identified in a personal interview as users of alternative care will again be interviewed in the home. The study will identify the reasons for alternative care by rural poor and black elderly and provide clues as to the dynamics of their health care utilization.

"Use of Perinatal/Infant Services by Hispanics in AHCCS"
Patricia D. Moore, Ph.D., Arizona State University, Grant No. HS06127

Mexican-Americans have been shown to have lower use rates of prenatal care and well baby care, even when financial and providers barriers have been lowered. This study will evaluate the effects of acculturation, family function, and past experience on the utilization of preventive services for a group of Mexican-Americans and whites enrolled in the Arizona state Medicaid HMO called AHCCS. Results are expected to assist in designing more effective health care delivery system for this rapidly expanding population of Americans.

Intramural Research

A major component of the Agency's intramural research program is the National Medical Expenditure Survey (NMES). Results of this survey will provide the Federal Government with current information on how much Americans use, pay for, and finance medical care.

The 1987 NMES was designed to meet the nation's need for analyzing health expenditures and public and private insurance programs. By extending data collection to the institutionalized population and by oversampling population groups of particular interest of Federal policymakers, NMES data can be used to examine a far broader range of issues than any preceding survey. Estimates based on NMES data can be employed to assess the general impact and specific effects of current programs and the potential impact of proposed legislation on the cost and use of health services across all sectors of the health care delivery system.

The 1987 NMES gathered data from a national probability sample of the civilian noninstitutionalized population. The NMES sample of approximately 14,000 civilian households (37,000 persons) includes oversampling of groups of particular policy interest: Blacks, Hispanics, the poor and nearly poor, the elderly, and persons with functional limitations. It also includes a sample of American Indian and Alaskan Native households.

The NMES Household Survey was a year-long panel collecting measures of health status, use of health care services, expenditures and sources of payment, insurance coverage, employment, income and assets, and demographic information. Household data will be supplemented by surveys of medical health insurance providers, employers, and insurers associated with the sampled persons, and by data from Medicare administrative files.

The following papers on minority health concerns were presented at the 1989 American Public Health Association annual meeting by staff of the National Medical Expenditure Study:

Authors: Peter Cunningham
Title: Health Care Coverage of Native Americans

Authors: Karen Beauregard
Title: Access to Health Care Among Native Americans

Authors: Doris Lefkowitz
Title: Medicaid Eligibility and the Use of Preventive Services by Low Income Children

Authors: Lee Cornelius
Title: Access to Medical Care of Black, White and Hispanic Children: a 1987 Profile

Authors: Ayan Johnson
Title: Chronic Disease: Comparison Between American Indians and Alaska Natives and the U.S. Population

Authors: Carol Underwood
Title: Personal Health Practices Among Native Americans

MULTIPLE SCLEROSIS
Obligations

	1987	1988	1989	Estimate 1990	Estimate 1991
Public Health Service:					
National Institutes of Health:					
National Institute of Neurological Disorders and Stroke.....	$43,039,000	$48,172,000	46,255,000	47,731,000	49,929,000
National Institute of Allergy and Infectious Diseases.....	21,663,000	20,488,000	6,385,000	6,541,000	6,898,000
National Center for Nursing Research.....	16,000	---	---	---	---
Office of the Director, NIH 1/.....	76,000	54,000	105,000	---	---
TOTAL, NIH.....	64,794,000	68,714,000	52,745,000	54,272,000	56,827,000

1/ Represents funds awarded through BIDs for Academic Research Enhancement Awards.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Disorders and Stroke

MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is a central nervous system disease that is unpredictable and often crippling. It is unpredictable because its course can be relatively benign, somewhat disabling, or devastating. It is crippling because communication between the brain and other parts of the body is disrupted, at worst leaving the person unable to speak, walk, or write.

No one knows exactly how many people have MS. In the United States, estimates range from less than 200,000--derived from physician and hospital records--to 500,000--derived from estimates based on public surveys and pathology specimens.

During an MS attack, inflammation occurs in various areas of the central nervous system in random patches called plaques. This process is accompanied by loss of myelin, a fatty covering that insulates nerve cell fibers in the brain and spinal cord and facilitates the smooth, high-speed transmission of electrochemical messages between these components of the central nervous system and the rest of the body. When myelin is damaged, neurological transmission may be slowed or blocked completely, leading to diminished or lost function.

Symptoms may be mild or severe, of long duration or short, and may appear in various combinations, depending on the area of the nervous system affected. The initial symptom is often blurred or double vision, even blindness. Nearly all MS patients at some time experience numbness and muscle weakness in their extremities, and difficulty with coordination and balance. These symptoms may be severe enough to impair walking or even standing. Speech impediments, fatigue, tremors, and dizziness are other common complaints. As the disease progresses, sexual dysfunction may become a problem. Bowel and bladder control may also be lost. Some patients experience memory impairment and depression.

Most commonly, MS first manifests itself as a series of attacks of nervous system dysfunction followed by complete or partial remissions as symptoms mysteriously come and go. The least severe 20 percent of the MS population has a benign form of the disease in which little or no progression occurs following the initial attack. In some patients, however, MS becomes chronic and progressive: the course of the disease is unrelieved by remissions, and symptoms steadily worsen. Usually this progression is slow, but for some chronic progressive patients, the decline is swift and relentless, rendering them totally

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disabled. In some patients MS may take the chronic progressive form from the onset.

Most people with MS learn of their disease between the ages of 30 and 50. Women are almost twice as likely to develop MS as men; whites more than twice as likely as other races. The erratic symptoms of MS can affect the functioning of the entire family, as patients may become unable to work at the same time that they face high medical bills and additional expenses for housekeeping assistance and modifications to homes and vehicles. The emotional drain on both patient and family is unmeasurable.

No definitive test is yet available to diagnose MS. When faced with a patient whose symptoms and neurological examination suggest MS, physicians use a variety of tools to rule out other possible causes, such as a brain tumor or stroke. Imaging technologies like magnetic resonance imaging (MRI) and computerized tomographic scans can help locate central nervous system lesions resulting from myelin loss, but these lesions can be encountered in several other neurological disorders and are not absolute evidence of MS. Evoked potentials tests--which measure the speed of the brain's response to visual, auditory, and sensory stimuli--can sometimes detect lesions the scanners miss. Like imaging technologies, evoked potentials are helpful but not diagnostic, as they cannot disclose the cause of lesions. The physician may also study the patient's spinal fluid for cellular and chemical abnormalities often associated with MS.

Although its cause remains unknown, many scientists believe MS to be an autoimmune disease--one in which the body's defense system is abnormal, reacting against the nervous system--possibly related to an environmental trigger, perhaps a virus. There is increasing evidence that genetics may play a role in determining susceptibility to MS. A great deal of interest is also focused on the blood/brain barrier, which controls the passage of substances from the blood into the central nervous system. In MS, it is possible a harmful substance is getting by this barrier and causing nervous system damage.

A Coordinated Attack

Within the Federal Government, the National Institute of Neurological Disorders and Stroke (NINDS) is the focal point for the national research effort against MS. Several other NIH components--the National Institute of Allergy and Infectious Diseases; the National Cancer Institute; the National Heart, Lung, and Blood Institute; the National Center for Nursing Research; and the Division of Research Resources--also support MS research. Other Federal agencies with interest in this field of research are the Centers for Disease Control, the Veterans Administration, the National Science Foundation, the National Institute of Disability and Rehabilitation Research, and the Department of

Defense. In the private sector, the National Multiple Sclerosis Society supports research and provides a wealth of information and services to patients and their families.

The Search for an MS Virus: Narrowing the Field

Many investigators believe a virus may be involved in the cause of MS, but no one has been able to pin the blame convincingly on one specific virus. Particular interest is being focused on a viral subgroup called retroviruses, ones whose genetic code is written in RNA (ribonucleic acid) rather than DNA.

A team of NINDS intramural investigators has reported findings that appear to exonerate the retroviruses known as human T lymphotropic viruses (HTLV-I, -II, and -III) as common causal agents. Drs. David L. Madden, Marinos C. Dalakas, John L. Sever, and Ms. Nancy R. Tzan investigated the frequency of antibodies to HTLV-I, -II, and -III in the blood and spinal fluid of MS patients and matched control individuals, including patients with other neurologic diseases. (Antibodies are proteins made by the immune system that bind to structures they recognize as foreign--i.e., antigens.) The team was unable to find significant levels of antibodies to HTLV in any of the people tested. Similar results were reported by NINDS grantee Dr. Gary Birnbaum at the University of Minnesota School of Medicine in Minneapolis, who studied the spinal fluid of MS patients and people with other neurologic diseases for evidence of infection with HTLV-I.

Other investigators focused on coronaviruses, since particles of this viral family produce demyelinating diseases in animals and have been found in the brains of MS patients. Drs. John O. Fleming and Leslie P. Weiner, NINDS grantees at the University of Southern California in Los Angeles, used monoclonal antibodies for several types of coronaviruses to study the blood and spinal fluid of MS patients, normal controls, and people with other neurologic diseases. (Monoclonal antibodies are antibodies harvested from cells descended from a single cell so that they are identical and highly specific for a single target.) The research team found no significant differences in antibody responses among the three groups.

While these studies do not rule out a possible role for HTLV and coronaviruses in the etiology of MS, they do suggest that such viruses are not likely to be significant contributing factors.

At the University of California, Los Angeles NINDS grantee Dr. Roger Detels and his colleagues studied 145 people with MS to determine whether the development of the disease might be associated with exposure to uncommon viruses or with late-age exposure to common viruses. One hundred forty five healthy

friends of the MS patients--matched for race, sex, approximate age, birthplace, and geographic area--served as a control population. Dr. Detels found that the MS patients were much more likely to have had infectious mononucleosis than the control group. They also changed residences more frequently, were more likely to have lived on a farm, and to have traveled to Mexico (a common destination for participants in this West Coast-based study). All three factors could have resulted in more opportunities for infection by a number of viruses. Among the female participants, MS patients reached menarche earlier than their healthy friend-controls. This finding could support the theory that late childhood or post-pubertal infection with common viruses may play a part in the onset of MS. The investigators do not interpret the higher prevalence of infectious mononucleosis as evidence of a specific etiologic link to MS. Rather, they propose that this reflects the observation that many viruses have been implicated in the cause of MS and suggests that a number of different viral agents, acting alone or together, may trigger an autoimmune response leading to the disease.

Implicating Cells of the Immune System

The body's immune system, which is believed to behave abnormally in MS, embraces many kinds of cells. One important group develops in the thymus and is known therefore as T-cells. NINDS grantees Drs. Howard L. Weiner and David A. Hafler at Harvard Medical School in Boston, Massachusetts have found that chronic progressive MS patients have decreased numbers of certain T-cells known as suppressor/inducers, which tell the immune system when to reduce its activity. In these patients, the system that protects against disease does not adequately turn off. The scientists also studied control populations comprised of healthy people and patients with neurological diseases other than MS, and discovered similar results: individuals with low numbers of suppressor/inducer T-cells did not adequately turn off immune system activity. Drs. Weiner and Hafler propose that measurement of suppressor/inducer cells provides a way to monitor immune system suppression in chronic progressive MS patients.

Defining the Role of Genetics

There is growing belief among scientists that heredity may play a role in the etiology of MS. Studies of twins have shown that when one develops MS, the other is more likely to also have MS if the pair are identical, rather than fraternal, twins. But the rate for identical twins both developing MS is significantly less than 100 percent, indicating that expression of the disease is not entirely genetically controlled. Also, since fraternal twins, who do not inherit identical gene pools, have a lower rate for both siblings developing MS than identical twins, it may be that more than one gene is involved in MS susceptibility.

Other indications of a possible genetic connection come from animal studies: strains of mice with missing T-cell receptor-gene segments are more susceptible to demyelinating diseases than other strains.

To explore the role of genetics in people with MS, NINDS intramural scientists Drs. Steven S. Beall, Henry McFarland, Dale E. McFarlin, and William E. Biddison, working with colleagues at the California Institute of Technology in Pasadena and the University of California in Los Angeles, studied genetic characteristics of MS patients and two control populations to determine what differences might exist between them. The MS patients had the chronic progressive form of the disease. The first group of controls were healthy volunteers. The second control group consisted of healthy volunteers with high levels of an antigen called DR2. MS patients express DR2 markers more often than the general population, and the inclusion of this second group controlled for its possible effects.

The investigators found no difference in prevalence of T-cell receptor genes in the three groups, but certain combinations of these genes occurred more frequently in the MS patients than in either control group. The data indicate that the risk of developing MS is more than three times greater than normal for people who have both the abnormal gene combination and the DR2 marker. (These findings have now been confirmed by an independent group of investigators and are further described in the section of this report by the National Institute of Allergy and Infectious Diseases.)

The scientists speculate that several genes--two for T-cell receptors and at least one for DR2 antigen--may combine to determine risk of developing MS. It is also possible that these abnormalities may represent a link to an as yet undiscovered MS susceptibility gene or that abnormal immune system function in MS patients could lead to either aberrant or missing expression of some genes. Further studies will attempt to determine which of these theories may be correct.

Animal Models Provide Clues to Immune Function

Since much of our understanding of the immune system comes from studies of animals, scientists continue to refine animal models of demyelinating disease. It is now possible to induce inflammation and demyelination in susceptible mice by transferring special T-cell lines grown in tissue culture into the rodents. The resultant disease--called chronic relapsing experimental allergic encephalomyelitis (CREAE)--shares many characteristics with MS; however, the mechanisms by which CREAE is initiated are not yet known.

course of MS; however, toxic side effects preclude their widespread use. Studies of steroids suggest intravenous methylprednisolone may be superior to the more widely used ACTH for the treatment of exacerbations.

o Methods to Monitor the Disease Process--MRI studies show that asymptomatic lesions can come and go frequently, and that chronic progressive patients accumulate new enlarging lesions faster than relapsing/remitting patients. The use of gadolinium, a contrast agent that enhances MRI scans, aids in the identification of lesions involved in a breakdown of the blood/brain barrier and helps distinguish new lesions from old. This ability may prove valuable in determining the efficacy of new therapies.

o New Insights into Biological Mechanisms--Studies of T-cell triggering and immunoregulatory mechanisms are providing insights into new targets for both therapy and genetic linkage studies. Also under investigation are cells--endothelial, astrocytic, and microglial--that may be involved in the migration of harmful molecules across the blood/brain barrier into the central nervous system.

o New Therapeutic Approaches--Since the conduction of electrochemical messages is compromised in MS, medications to improve conduction are also under study. One such drug, 4-aminopyridine, has been shown to have temporary beneficial effects. Investigators are also beginning to look at the possibility of developing an MS vaccine. In one preliminary trial, T-cells were separated from the spinal fluid of two MS patients, cloned and grown in the laboratory, inactivated and injected back into the patients. The participants tolerated the treatment well and without toxic side effects. Monoclonal antibodies directed against subsets of cells in the immune system have resulted in some success in treating animal models of MS, although humans' adverse reactions to the antibodies (which are made from mouse proteins) preclude their widespread use. Certain connective tissue cells, known as mast cells, may contribute to inflammation, a characteristic of MS. In animal models of autoimmune disease, anti-mast cell drugs have shown beneficial effects.

o Strategies to Reverse the Damage--Both myelin and oligodendrocytes (the cells that make and maintain myelin in the central nervous system) are destroyed during exacerbations. Scientists now know that oligodendrocytes may proliferate and form new myelin after an attack. Therefore, there is a great deal of interest in agents that may stimulate this remyelination. To learn more about the process, investigators are looking at the effects drugs used in MS trials have on remyelination. Studies of animal models indicate that the immunosuppressants cyclophosphamide

and azathioprine may accelerate remyelination, while steroids may inhibit it.

Clinical Trials of Drugs to Treat MS

The Georgia conference is indicative of the extensive efforts underway to develop treatments for MS. These therapies remain experimental and a treatment that is beneficial to all patients has not yet been found. Many studies involve agents that regulate or suppress the immune system.

Interferons as Immune System Regulators

One of the most promising MS research areas involves naturally occurring antiviral proteins known as interferons. Clinical trials of three different types of interferon--alpha, beta, and gamma--have shown that the first two may exert some beneficial effect on the clinical course of MS, while gamma interferon significantly increases the exacerbation rate. These findings prompt investigators to ask what role, if any, interferons play in the development of the disease.

To explore this question, NINDS grantee Dr. Ute Traugott at the Albert Einstein College of Medicine in the Bronx, New York studied central nervous system tissue specimens obtained during postmortem examinations of MS patients, normal control subjects, and patients with other neurological diseases. Interferons were virtually absent from the tissue of normal controls, bu did show up in tissue from patients with some neurological diseases other than MS. In tissue from MS patients, Dr. Traugott found that interferons were detectable only in lesions associated with active disease processes. Furthermore, the distribution patterns of alpha, beta, and gamma interferon differed depending upon whether the disease state was chronic or acute.

Dr. Traugott also found evidence indicating that gamma interferon may be involved in the growth of MS lesions, while alpha and beta interferon probably exert a suppressive effect on the immune system. It is worth noting that in several MS patients who also had viral pneumonia, gamma interferon was extensively distributed; MS patients with septicemia, a bacterial infection of the blood, showed limited distribution of gamma interferon. These findings strengthen the theory that MS is triggered by viral, not bacterial, infections and suggest that viral infections and the resulting immune response may serve to activate MS.

Therapies to Suppress the Immune System

--Cyclosporine

NINDS intramural scientist Dr. Henry McFarland contributed to one of the largest MS clinical trials to date, studying 48 patients with chronic progressive MS as part of a multi-center investigation of the immunosuppressive drug cyclosporine. Initial results from the NINDS laboratory and other participating centers indicate cyclosporine may be beneficial in the treatment of chronic progressive MS patients, but at the present time the drug cannot be used due to significant side effects, especially kidney damage. This study generated a great deal of new information on the natural course of chronic progressive MS.

--Azathioprine

Dr. George Ellison and his colleagues at the University of California, Los Angeles also undertook a clinical trial of azathioprine as a treatment for MS. Patients with chronic progressive MS were randomly divided into three groups. One group was given azathioprine and, for the first 36 weeks of the trial, methylprednisolone. The second group received azathioprine and a placebo; the third received two placebos. After three years, there was no statistically significant difference in the rate of progression (the degree to which symptoms worsen) among the three groups of patients. Both groups receiving azathioprine had half as many relapses (acute attacks). However, the risk of adverse side effects associated with both drugs were found to outweigh the benefits. Therefore, the investigators do not recommend azathioprine, with or without steroids, to treat chronic progressive MS patients.

--Plasma Exchange

Plasma exchange is a process whereby various elements are separated from a patient's blood and the blood is reinfused into the patient. The ability to remove antibodies and other immunologically active substances from blood has led to the use of plasma exchange as a therapy for several neurological conditions in which autoimmunity is believed to play a role. Several pilot trials of plasma exchange in MS have reported positive clinical results.

NINDS grantees Dr. Howard L. Weiner at Harvard Medical School in Boston, Massachusetts and Dr. Gary Birnbaum at the University of Minnesota in Minneapolis organized a formal cooperative study to determine the efficacy of plasma exchange to enhance treatment of MS exacerbations. Both relapsing/remitting and chronic progressive MS patients, all experiencing exacerbations, were admitted to the study. Half of each group underwent true plasma exchange; the control patients participated in a simulated

exchange. All patients received ACTH and cyclophosphamide. The scientists observed no long-term benefits, although there was modest evidence that plasma exchange, in conjunction with ACTH plus cyclophosphamide, may enhance recovery from an MS attack in relapsing/remitting patients over the short run.

Monitoring Disease Activity

The erratic course of MS makes it hard to evaluate treatment. Since remissions and exacerbations take place sporadically and unpredictably, it is difficult to assess whether improvement is due to the experimental therapy or to a naturally occurring remission. Therefore, investigators are seeking reliable, objective methods to measure disease activity.

While studying methylprednisolone and azathioprine, Dr. Ellison and his colleagues used evoked potentials tests to monitor the drugs' effectiveness. Evoked potentials are tests that measure the time it takes for an electrical impulse to travel from the nerves of the eye, ear, or skin to the brain. These tests can sometimes detect so-called "silent" lesions that do not produce physical symptoms.

Changes could be detected by evoked potentials a full year before they showed up in the standard neurological exam, suggesting the possible usefulness of these tests as predictors of clinical changes. Also, unlike neurological exams or disability scale ratings, evoked potentials are objective measures of change. Dr. Ellison believes these tests, especially the visual type and those that evaluate sensing functions of the body are a good tool for measuring disease progression and the effectiveness of treatments in MS patients. They are not, however, a good measure of disease activity.

Such a measure is being sought by Dr. John N. Whitaker, an NINDS grantee at the University of Alabama in Birmingham, who has developed a way to detect myelin basic protein (MBP) fragments in urine. It is known that when myelin is damaged in the central nervous system, MBP-like material enters the spinal fluid and urine. In several spinal fluid studies, MBP levels have been found to correlate well with the severity of the demyelinating process. The advantages of the new urine test are that it would spare the patient the invasive procedure required to obtain spinal fluid and that it would permit frequent analyses. So far, however, the concentration of MBP does not appear to correlate with clinical disease activity. Dr. Whitaker plans further studies to try to characterize the myelin fragments, leading to better understanding of how the body processes MBP outside the myelin sheath.

Controlling Spasticity

With NINDS support, scientists are searching for new and better medications to control the symptoms of MS without triggering intolerable side effects.

Grantee Dr. Richard A. Rudick at the Cleveland Clinic in Ohio studied the drug progabide in 25 MS patients with spasticity. Progabide has been shown to reverse spasms in rats and monkeys. Dr. Rudick found that progabide lessened the patients' spasticity, especially in the legs, and unlike the antispasmodics baclofen and diazepam, was not associated with weakness in the muscles. Many patients complained of feeling drowsy, dizzy, or nauseated, but these problems cleared up when the progabide dosage was decreased. More worrisome was the appearance in seven patients of liver damage. This toxic effect resolved spontaneously after progabide was discontinued, but precludes use of the drug until this problem can be controlled.

Cognitive Functions in MS

Dr. Stephen M. Rao, an NINDS grantee at the Medical College of Wisconsin in Milwaukee, is studying neuropsychological aspects of MS. It has been suggested that lesions seen on MRI scans of asymptomatic people with MS may be associated with cognitive defects. Dr. Rao and his colleagues found that the greater the total lesion area in the brain (as visualized by MRI), the more likely the person is to have deficits in recent memory retrieval, abstract and conceptual reasoning, language, and visuospatial problem solving. MRI scans also point to a positive correlation between the degree of atrophy of the corpus callosum--the bridge that connects the left and right hemispheres of the brain--and poor performance on tasks requiring sustained attention and rapid problem solving. In fact, severity of corpus callosum atrophy appears to be a better predictor of reduced speed and accuracy than measurements of total lesion area. The investigators hypothesize that these tasks may depend on interhemispheric communication that is disrupted by demyelinated callosal fibers. Dr. Rao did not find any correlation between duration of illness and severity of cognitive dysfunction.

The Epidemiology of MS

Because symptoms of MS do not usually appear until the adult years, it is very difficult to ascertain whether any factors associated with the patient's birth or youthful years influence the subsequent development of the disease. Suitable records for retrospective studies are rarely available, and since MS is relatively uncommon and cannot be reliably predicted, prospective studies are not feasible.

However, NINDS intramural scientist Dr. Gerald L. Stoner is pursuing a unique opportunity to study the influence of perinatal factors. Between 1959 and 1965, the NINDS sponsored a Collaborative Perinatal Project at 14 U.S. hospitals. Data were collected on 55,000 pregnant women during their pregnancies, at the time of delivery, and six weeks later. At the same time, in a similar but independent study, the Kaiser Foundation collected data on 20,000 pregnant women seen at its hospital in Oakland, California. In both studies, data on the offspring were collected during neurological and developmental examinations when the children were one and seven years of age.

It has been estimated that as many as 45 of the mothers and 20 of the children may have already developed MS symptoms. What makes the offspring of these women so important is that for the first time scientists have the detailed records needed for a retrospective study of the role of perinatal factors in MS.

The NINDS also has three to five frozen serum samples from each of the women studied. Dr. Stoner believes that the sera provide a unique opportunity to examine how primary viral infections or viral reactivations occurring in a woman during pregnancy may influence subsequent development of MS in the child. Sera from the women in the Kaiser Child Health and Development Study are also available through the National Institute of Child Health and Human Development.

Dr. Stoner is encouraging physicians to bring this study to the attention of any MS patients they see who were born or gave birth between 1959 and 1965 at one of the participating hospitals. The National Multiple Sclerosis Society is also encouraging MS patients who may have been included in either the Collaborative Perinatal Project or the Kaiser study to contact Dr. Stoner.

National Institute of Allergy and Infectious Diseases

Inheritance of T-cell Receptor Gene Linked to MS Susceptibility

Multiple sclerosis may be considered an autoimmune disease because it involves an attack on tissues of the nervous system by a person's own immune cells. T-cells play an important role in this attack. Activated T-cells are commonly found in lesions in the brain and in nervous system fluids taken from people who have MS.

NIAID-supported researchers studying the role of the immune system in the development of MS have found that certain genes influence susceptibility to this debilitating disease.

T-cell activation is triggered by molecules, called T-cell receptors (TCR), located on the cell's surface. These receptors are controlled by two sets of genes, alpha and beta, located in the cell's nucleus. Each gene set consists of different segments that rearrange in a particular way depending on which type of defense against microbes the body needs.

NIAID researchers are exploring the role these TCR's play in the development of MS. Recently, Drs. Thomas Kindt and Mary Ann Robinson, in the NIAID's Division of Intramural Research, in collaboration with NINDS grantee Dr. Stephen Hauser and his colleagues at the Massachusetts General Hospital in Boston, showed that certain inherited forms of T-cell receptor beta (TCR-beta) genes may render a person more susceptible to MS. These forms may inappropriately trigger T-cells to attack the body's own nervous system tissue.

The researchers studied TCR-beta genes in families in which two or more siblings had MS. Everyone has two copies of TCR-beta genes; children inherit one copy from each parent. Using molecular probes, the researchers tracked the TCR-beta genes from each parent to their children. This allowed the researchers to tell which of each parent's two copies of the genes the children inherited.

The siblings with MS tended to inherit the same form of their parents' TCR-beta genes, whereas non-affected siblings inherited a random mix of the genes. Work is now underway to determine the exact chromosomal location of the gene within the TCR-beta group that may underlie susceptibility to MS. The scientists will then study it for abnormalities that could cause T-cells to attack the body's own nerve cells.

Although inheritance of certain TCR-beta genes appears to make some people susceptible to MS, these genes are not the sole cause of the disease. Many researchers believe that slowly

activating virus infections, acquired in early childhood, may also play a role.

Viruses Attacking the Brain May Hide from the Immune System

A continuing quest by NIAID-supported researchers is to understand how viruses that infect the nervous system also elude the immune system. This trait allows some viruses to establish persistent infections that slowly undermine the brain's delicate biochemical harmony.

NIAID grantee Dr. Stephen Udem, at the Albert Einstein College of Medicine in New York City, and his coworkers have recently discovered clues that will help answer that question. The researchers studied children who had a neurologic disease different from MS, known as subacute sclerosing panencephalitis (SSPE). This progressive disease is caused by a measles virus that slowly replicates in the brain.

Scientists have observed that brain cells from children with SSPE contain large numbers of virus particles inside the cells, but little evidence of infection outside the cells. Cells that contain replicating viruses typically display newly made virus particles on their surfaces. These surface particles alert the immune system to the infection.

Dr. Udem's research team sought to determine why brain cells of SSPE patients didn't appear to produce new virus particles. Although the brain cells of these patients appeared normal, the researchers found that the virus genetic material, which controls replication of those measles viruses, contained abundant mutations. Even small mutations in virus genetic material, the researchers found, can result in defective viruses unable to make their way outside the cell. Without newly made virus particles on the cell surface, the immune system was unable to detect the virus infection. By evading the immune system in this way, mutations in virus genetic material may allow the infection to persist for many years, slowly tilting the balance of normal nervous system function.

Scientists have yet to prove whether measles virus or other viruses that attack the nervous system actually cause MS. However, a new biotechnology tool called polymerase chain reaction will help scientists sift through the genetic material of people affected with MS and identify material from viruses or other foreign organisms. Dr. Udem and others have begun to use this technique to look for foreign genetic material in people with MS.

Future Research Directions

It has been over a century since the clinical manifestations of MS were first described. In that time, scientists around the world have learned a great deal about this perplexing disease. Basic laboratory research has allowed investigators to study the process of demyelination on a cellular level. Animal models have provided leads to genetic, immunologic, and clinical avenues of research. A number of treatment ideas have reached the stage of clinical testing after early, painstaking work in the laboratories.

Basic and clinical scientists are continuing to investigate MS in a search for leads to additional research. They are working to gain more knowledge about this formidable disorder--knowledge that will someday eradicate MS forever.

CENTERS FOR DISEASE CONTROL

National Center for Health Statistics

MULTIPLE SCLEROSIS

According to the 1987 National Hospital Discharge Survey (NHDS), in 1987 an estimated 26,000 patients were hospitalized in short-stay hospitals in the United States with a first-listed diagnosis of multiple sclerosis. The average length of stay for these patients was 9.7 days. About 81 percent of these discharges were females and 73 percent of the patients with a first-listed diagnosis of multiple sclerosis were between the ages of 15-44 years. In addition to those patients with a first-listed diagnosis of multiple sclerosis, an estimated 34,000 patients were discharged with a secondary diagnosis of multiple sclerosis. These are patients who had another diagnosis listed as first or principal but had multiple sclerosis also shown on their medical records.

RURAL HEALTH

Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
Public Health Service:					
Health Resources and Services Administration	202,643,000	222,078,000	304,638,000	330,097,000	325,380,000
NIH:					
National Cancer Institute	---	---	13,947,000	14,537,000	14,801,000
National Institute of Environmental Health Sciences	---	---	---	740,000	740,000
National Institute on Aging	---	---	1,785,000	2,285,000	2,325,000
National Library of Medicine Outreach	---	---	1,800,000	3,800,000	3,800,000
National Institute for Nursing Research	---	---	1,461,000	2,000,000	2,000,000
Subtotal, NIH	---	---	18,993,000	23,362,000	23,666,000
Alcohol, Drug Abuse, and Mental Health Administration	1,573,000	1,566,000	7,010,000	10,080,000	9,470,000
Centers for Disease Control	1,600,000	1,600,000	1,600,000	13,052,000	13,029,000
Agency for Health Care Policy and Research	290,000	300,000	679,000	2,489,000	2,500,000
TOTAL, PHS	206,105,000	225,544,000	332,920,000	379,080,000	374,045,000

HEALTH RESOURCES AND SERVICES ADMINISTRATION
Bureau of Health Professions

Rural Health

In FY 1989, most Area Health Education Center (AHEC) projects were involved either wholly or in part with rural health activities. Twelve of the projects received a total of $4,021,114. The University of Arkansas received the largest award ($1,543,105) for their AHEC rural health training involving 30,000 students, residents, and population of the service area. The clinical training, education and health services emphasized through AHEC rural health activities are estimated to affect approximately 2,123,420 individuals, many of whom are underserved populations.

Under section 786(a) Family Medicine programs, 14 predoctoral and 25 graduate training programs indicated some rural health oriented training activities. The residency training program grantees received a total of $146,717 which will enhance the clinical training of approximately 222 residents.

Nursing programs support projects implementing outreach programs making basic advanced and continuing nurse education programs accessible to individuals and providing rural clinical practicums for nursing students. During Fiscal Year 1989, the Advanced Nurse Education Program provided $376,964 to 3 projects designed to prepare nurses at the graduate level to provide expert clinical care, particularly in acute care settings, and to prepare teachers and researchers in this important area. The Nurse Practitioner and Nurse Midwifery Program funded 5 grants for $927,037 which would prepare family nurse practitioners and nurse midwives specifically to work in rural areas of the country. In 1989 the Nursing Special Projects program supported 20 projects for $2,543,948 to increase the supply of adequately trained nursing personnel to meet the health needs of rural areas.

Approximately 742 students in 24 Physician Assistant Training programs benefited from the rural health activities supported by grants in the amount of $69,785.

Four General Internal Medicine/General Pediatrics Residency programs offered rural health training experiences for eight residents. No specific funds were identified for this purpose.

One Podiatric Primary Care Residency Training program grantee reported rural training emphasis for eight residents. The College of Podiatric Medicine and Surgery in Iowa received $10,477 specifically for this purpose.

Rural health care will be included in the training of 6 fellows at two projects supported under the Geriatric Medicine and Dentistry Faculty Training program.

Two AIDS Regional Education and Training Center projects have indicated training targeted toward rural health issues.

In FY 1989 an $800,000 contract was awarded to study the supply of health professionals and whether such supply is adequate to meet the demands for health care services in rural communities.

In FY 1989, $1,360,000 was awarded to 4 geographically unique rural hospitals under the Ad Hoc Hospital Grants, P.L. 100-607. These funds were used for advancement of health care services and the enactment of quality care.

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HEALTH RESOURCES AND SERVICES ADMINISTRATION

Office of Rural Health Policy

Rural Health

The Office of Rural Health Policy (ORHP) was established within the Health Resources and Services Administration in August 1987 and authorized by Congress in December 1987. The major responsibility of the office is to work within the Department and with other Federal agencies, States, national associations, foundations, and private sector organizations to seek solutions to health care problems in rural communities.

During FY 1989, ORHP renewed grant awards to continue operations of the five Rural Health Research Centers. These Centers collect and analyze information, conduct applied research on rural health issues, and widely disseminate the results. The center directors met twice to collaborate and share information.

The National Advisory Committee on Rural Health held three meetings during the past year and submitted its annual report, with recommendations, to the Secretary in November. The purpose of this committee is to advise the Secretary on the priorities and strategies that should be considered for addressing the issues and unique problems related to providing and financing health care services in rural areas. Staff support to the committee was provided by ORHP. The office continued to manager a 3-year demonstration grant to Texas Tech University that is establishing an interactive satellite-based video communications system and data exchange between teaching hospitals and rural physicians in West Texas.

In FY 1990, ORHP will continue to monitor performance of the five Rural Health Research Centers. Two additional grants will also be awarded to support research with an emphasis on health problems of rural minorities and rural occupational health and safety. The office will provide staff support to the Advisory Committee as well as continued management of the telecommunications demonstration. The National Clearinghouse on Rural Health Information will become fully operational in cooperation with the National Agricultural Library, USDA.

ORHP will also conduct a number of significant special projects related to improving access to health care in rural areas.

NATIONAL INSTITUTES OF HEALTH

National Cancer Institute

RURAL HEALTH

The National Cancer Institute (NCI) has a number of activities in progress to assess the magnitude of cancer risk related to pesticides in rural agricultural areas. Evidence for an association between cancer risk and exposure to pesticides comes mainly from occupational studies. Leads for special studies and analyses of farmers and other persons with frequent exposure to agrichemicals have come from the analysis of cancer mortality data using mapping techniques and multivariate statistical methodology. In the late 1970's, NCI's Division of Cancer Etiology began a series of analytic correlation studies to investigate whether the county-by-county variation for individual cancers was related to demographic, industrial, or other county indices. In general, urbanization was a major determinant of the county rates for a majority of cancers, even after adjusting for other demographic factors. For some cancers, such as leukemia, high rates were observed in the Midwest in predominantly rural areas.

These data, coupled with information from the agricultural census, subsequently led to several etiologic studies of farmers and related occupational groups to investigate the relationship between chemical exposure and cancer risk. The results of these studies show that overall mortality among farmers is generally lower than that of the national average for all cancer sites combined. Nevertheless, surveys of occupational groups and studies of specific tumors suggest that farmers may have elevated incidence and mortality rates for certain cancers. These include cancers of the lymphatic and hematopoietic system, lip, stomach, prostate, skin (non-melanoma), brain and connective tissue. Other cancers, such as colon, rectum, liver, nose, lung and bladder tend to be low for farmers, while cancers of the skin (melanoma), esophagus, pancreas, testis and kidney show a generally inconsistent pattern. NCI studies of related occupations (e.g., veterinarians, pesticide applicators, etc.) also support the observed excess risk of cancer found with increased exposure to agricultural chemicals.

Approximately 65 percent of all pesticides used in the United States in 1976 were used by farmers; 25 percent may have been applied by commercial applicators who typically have considerable contact with pesticides. Heavy pesticide use may account for some excess risk of cancer among farmers. The excess of leukemia among farmers suggests a link with pesticide exposure in regard to the suggestion of an increased risk of leukemia among pesticide applicators and producers and case reports of pesticide-related aplastic anemia and chromosome aberrations.

The strongest evidence for a pesticide effect comes from

population-based case-control studies of non-Hodgkin's lymphoma in Kansas and Nebraska, where farm herbicide use was found to be associated with this disease. Relative risk increased significantly with the number of days of herbicide exposure per year and with latency. Excess risk was found to be associated with the use of phenoxyacetic acid herbicides, particularly 2,4-D. In the Kansas study, soft-tissue sarcoma was not associated with exposure to herbicides, in contrast to reports from Sweden. It was, however, associated with exposure to insecticides, particularly those used on animals.

National Institute on Aging

Access to and affordability of medical and social services are particularly pressing problems for older people living in rural areas. In early 1989, the National Institute on Aging (NIA) convened a panel of experts in rural health care to respond to a congressional request for expanded research on the health and social needs of older rural residents and for the development of a special center on rural health care.

Based on the panel's deliberation, the NIA is soliciting applications for Exploratory Centers on rural aging and will shortly issue a request for applications to do research on such topics as changing sociodemographic and epidemiologic characteristics of the older rural population, aging rural people as resources, and the availability, utilization and quality of health care and other services to older people in rural areas.

National Center for Nursing Research

The National Center for Nursing Research (NCNR) research on rural health focuses on access to health care, nursing care delivery models in rural hospitals, and health care needs of certain populations, including high-risk mothers and infants, adolescents, minorities, and older persons. NCNR is also interested in fostering research addressing the clinical and basic science questions relating to differences in morbidity and mortality in rural populations.

One NCNR study focuses on high risk health behavior in rural adolescents. Dr. Cheryl S. Alexander, of The Johns Hopkins University School of Hygiene and Public Health, in Baltimore, Maryland, is studying behaviors that might increase the risk of sexually transmitted diseases and other health problems in adolescents in three rural Maryland counties. This study is more fully described in the NCNR contribution to the Moyer report on AIDS.

Other NCNR studies on rural health include: approaches for reducing risks for cardiovascular disease in rural school children; multiple sclerosis (MS) in rural areas; and home care for older adults in a rural area.

The NCNR is also funding studies through cooperative agreements with the Division of Nursing of the Health Resources and Services Administration to test innovative practice models for nurses in acute care hospitals, including hospitals in rural areas. The studies are expected to provide valuable information on practice issues for nurses in rural areas.

In late FY 1990 a research and demonstration program on community-based rural health care models for minority populations will be initiated, cosponsored by NCNR, the Agency for Health Care Policy and Research and the Division of Nursing. Research in this new program will be focused on expanding the scientific understanding of the health status, health care requirements, and effective health care delivery methods for rural maternal-infant and elderly populations.

National Library of Medicine

In 1988 the Senate Committee on Appropriations requested that the National Library of Medicine "develop an active outreach program to disperse [the latest scientific and technical findings] to rural and remote health care professionals, and devise a method of notifying these professionals of the availability of up-to-date information." A Panel on Outreach was subsequently convened by the Library, and a report was issued in August 1989 (Improving Health Professionals' Access to Information).

The Panel's report outlines steps to implement the Senate Committee's charge, looking eventually to put NLM's vast store of knowledge into the hands of every health practitioner in the country, with special emphasis on the needs of health professionals in rural and other underserved areas.

In FY 1990, using approximately $3.8 million provided by Congress for "outreach enhancement" of a number of NLM ongoing programs, the Library is 1) awarding increased funds to the Regional Medical Libraries ($1.3 million) to help them make minority and rural health professionals more aware of available information resources, 2) providing additional funds for Resource Access Grants and Training Grants ($1.7 million), the former directed primarily at small and medium-sized hospitals to which rural and other health-care professionals turn for access to biomedical publications and electronic bibliographic databases, and the latter to aid in training librarians and health professionals in underserved areas in the use of modern computer and communications systems; and 3) increasing publicity ($0.8 million) to promote the use of the Library's current products and services, with emphasis on reaching professionals in rural and other underserved areas.

ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION

NATIONAL INSTITUTE OF MENTAL HEALTH

RURAL MENTAL HEALTH

Introduction

In fiscal year 1989, the National Institute of Mental Health (NIMH) began to substantially increase its support for projects concerned with mental health problems of and services for rural Americans. Much of the FY 1989 increase was made possible because Congress provided additional funds for services research and data collection through a set aside in the annual alcohol, drug abuse, and mental health block grant. In FY 1990, further increases were provided by a targeted increase in research funding. A number of valuable projects are underway and additional ones are being planned.

Research Activities

A researcher at the University of Nebraska is developing and testing a comprehensive model that links changes in local economic conditions to depression, alcohol abuse, impairments of social roles brought about by these disorders, and help-seeking behavior. The researcher is also assessing how variations in informal support networks, access to formal services, and willingness to use social supports temper the psychosocial impact of economic events on individuals.

The research covers a period of economic decline that has had devastating effects on rural sections of the State most heavily dependent upon agriculture. Data are being collected through telephone interviews with a representative sample of 2,500 adults; of these, about 1,500 had been interviewed previously as part of an ongoing Nebraska Annual Social Indicators Survey. An additional 400 subjects are being selected for face-to-face interviews.

Research also is focusing on topics such as the delivery, organization, and financing of mental health services in rural and largely rural States. One new research project is concerned with rural homelessness in Ohio and provision of services to mentally ill rural residents. The aim of the study, being conducted at Ohio State University, is to replicate part of a survey of homeless people in Ohio that was originally conducted in 1984-1985. The original survey included both rural and urban populations. The intent of the newer study is to replicate only the rural portion of the survey in order to provide more descriptive data on rural homelessness than has previously been available and to assess changes in rural homelessness over the intervening years. The researchers will also survey providers of services to rural homeless mentally ill persons in 21 rural counties.

This part of the study will examine what services exist, how sufficient they are, and how they are used by homeless mentally ill persons. An estimated 200 service providers will be interviewed. It is expected that the Ohio study will provide data necessary for making improvements in rural mental health and human service delivery systems.

Under a special NIMH initiative to improve research capacities in State mental health agencies, researchers in the Oklahoma Department of Mental Health are examining the cost effectiveness of two different ways of providing twenty-four hour emergency mental health services in 20 central Oklahoma counties. A quasi-experimental design is being used to compare traditional inpatient care versus crisis residential care in addition to traditional inpatient care.

Researchers at the University of Pittsburgh are applying interorganizational theory to understand better contemporary systems of service for mentally ill and emotionally disturbed children and youth. Their study is conducted in three rural western Pennsylvania counties in which, as elsewhere in the United States, public services and funding are fragmented and dispersed among mental health, health, child welfare, educational, and juvenile justice agencies, along with auxiliary services provided by voluntary and church groups. By adopting an open systems framework for the study of organizations and conceptualizing interorganizational ties as parts of a set of networks, the researchers seek to extend knowledge of how adaptation and change occur in networks of child and youth-serving organizations. Of particular interest is how these organizations are affected by long-term trends toward continued reduction in governmental spending for services.

More youth-related rural mental health research is being conducted by a Minneapolis investigator who is studying the service and mental health needs of adopted adolescents in four largely rural states: Illinois, Iowa, Minnesota, and Wisconsin. The goal of this research is to gain a better understanding of factors associated with emotional and behavioral problems in adopted adolescents in order to enhance service delivery to those at risk. Data are being collected from random samples of adoptive parents, adoptive adolescents, and nonadopted siblings.

At the University of Wisconsin in Madison, one of five NIMH research centers on the organization, financing, and delivery of care for the severely mentally ill, research focuses on mental health services provided by public sector agencies in rural and small city environments. The major activities of the Center are the construction and use of a core data base that provides opportunities to address key theoretical issues in service delivery.

The data base will incorporate information on a year's experience of some 3,000 chronically mentally ill patients drawn from nine Wisconsin county systems. Data will include county and Medicaid expenditures, specialty mental health services, patient outcomes, and service system characteristics. Other research at the Center will focus on issues such as long-term service needs and organization of care for young adults with schizophrenic disorders, psychotropic medication and other treatments for severely mentally ill persons in nursing homes, and effects of interagency ties in rural mental health service delivery systems.

The Epidemiological Catchment Area Program (ECA) also concerns itself with rural mental health. The ECA program has provided, for the first time, basic descriptive information on the prevalence of mental disorders and treatment patterns among Americans. As part of the program, a representative sample of 20,000 non-institutionalized and institutionalized adult Americans in five communities (New Haven, Baltimore, St. Louis, North Carolina, and Los Angeles) was interviewed. Data were collected using the Diagnostic Interview Schedule, a standardized, highly structured questionnaire designed to be administered by lay interviewers and yield a diagnosis of major mental disorder by means of computer algorithm. Four of the ECA sites have a rural component, and one site (North Carolina) is predominantly rural.

A researcher at Yale University is using data from the NIMH ECA program and the National Institute of Alcohol and Alcohol Abuse's Established Populations for Epidemiologic Study of the Elderly project (EPESE). The investigator will use data from the Yale and Duke University sites of these studies to identify combinations of social statuses which increase the risk of depression in the elderly and examine how these risks change with age. The social domains to be analyzed include marriage, family, employment, neighborhood, and leisure activities. The research provides an opportunity to examine depression in the rural elderly as well as to compare risk factors between rural (Duke) and urban (New Haven) settings. Potential clinical benefits include the identification of high risk subgroups of the elderly that may be responsive to prevention and early intervention programs.

Another researcher at Yale is investigating rural-urban differences in rates of psychiatric disorder and service usage in children ages 6-11 in Connecticut. Data on prevalence of disorder and need for services from a sample of children in a rural and small town administrative health region in eastern Connecticut will be compared to data recently collected in the context of a needs assessment survey in the urban New Haven area.

The epidemiology of mental disorders in Puerto Rico is being studied by several researchers. The studies contain a representative sample of the island population and include rural/urban components in their analyses. One of the studies, in particular, is investigating the effects of a natural disaster, flooding and mud slides in a rural area, on the subsequent mental health of those exposed.

A genetic epidemiology study using the Virginia Twin Registry, which is being conducted by a researcher at Virginia Commonwealth University, also has a rural component. The majority of the twins and their parents reside in rural areas of Virginia and rural/urban is a sociodemographic component in the planned analyses.

A new NIMH activity in FY 1989 involved an invitation to State and territorial agencies to apply for Mental Health Statistics Improvement Program (MSHIP) grants. The grants, which were competitively awarded, are aimed at assisting agencies in their ability to enhance their data collection and research capabilities through adoption and implementation of MSHIP national data standards jointly developed by NIMH and the States. A total of 36 MSHIP grants were awarded. Fourteen, at a total cost of $1.5 million, went to largely rural states.

Education, Training, and Services

Recent survey research has indicated that farm families rank stress next to chemical exposure as their most significant health concern and that some 21 percent of rural residents report significant levels of depressive symptomatology. The Depression Awareness, Recognition, and Treatment (D/ART) Program, a major secondary prevention program, aims to improve the early identification, assessment, treatment, and clinical management of depressive disorders through a national educational campaign focused on three major target audiences: the general public, primary care providers, and mental health specialists. One component of D/ART is the Community Partnership Program which consists of alliances of consumer advocacy groups, public interest groups, services agencies, private businesses, and professional associations. The coalitions being developed will plan, implement, and expand the impact of D/ART community and professional education programs. The Community Partnership Program is operational in the rural areas of a number of states, e.g., Alabama, Alaska, California, Colorado, Florida, Indiana, Kansas, Michigan, Minnesota, Missouri, North Dakota, Ohio, Oklahoma, Pennsylvania, Tennessee, Texas, Utah, Virginia and Washington.

The D/ART program also provides professional training grants to support short-term training activities for health and

mental health practitioners on diagnosis and treatment of clinical depression. A number of these training programs are in states with substantial rural populations: Indiana, Minnesota, Illinois, Utah, Vermont, Michigan, and Iowa.

The University of Iowa clinical Training in Diagnosis/Treatment of Depression project will provide continuing education regarding epidemiology and assessment of depression; psychological and biological perspectives on the etiology of depression; psychological and biological interventions; case management; and special populations particularly affected by depression. Several methods of instruction will be used including lectures, audio-visual presentations and group discussions. The trainees will be 360-600 health and mental health professionals who practice in rural and agricultural areas affected by the farm crisis, primarily in Iowa. The program will be offered at 6 sites. The faculty will be multidisciplinary and will include psychologists, nurses and psychiatrists. The training provided is expected to increase the ability of the participants to appropriately diagnose and treat depression.

Because a primary care physician often is the only professional available in many rural areas, D/ART training being conducted at the University of Minnesota focuses on accurate assessment and management of major depression in adults by primary care physicians. At the University of Utah, the Mountain West Project is expected to train over 500 health and mental health practitioners from Utah, Idaho, Montana, and Wyoming on either the treatment of adults or the treatment of adolescents.

Work soon will be completed on an NIMH-supported evaluation of four rural mental health demonstrations. The demonstrations, funded in 1987, were aimed at improving mental health and other services in States most adversely affected by the farm crisis. All 13 eligible States applied for the grants that were awarded on a competitive basis to Iowa, Minnesota, Nebraska, and South Dakota. Each of the four demonstrations included activities at State and local service delivery levels.

The Future

In FY 1990, NIMH will use its Office of the Associate Director for Special Populations to undertake a number of initiatives to stimulate research programs and other activities relevant to mental health issues in rural populations. Early in calendar year 1990, several program announcements will be sent to appropriate academic departments in universities in states that have substantial rural populations. Included with the announcements will be invitations to submit applications that have as their major

emphasis the concerns of persons living in rural areas. To stimulate successful applications, NIMH will conduct intensive technical assistance workshops and preapplication consultation with applicants.

A workshop on the state of the art of mental health research pertaining to rural populations also will be conducted in fiscal year 1990 to assess where significant gaps in knowledge exist. A new research program announcement will be developed based on the outcome of the review.

NIMH also will include in all new requests for application a special note to applicants in the "Application Characteristics" section encouraging them to undertake research pertaining to rural populations. In the past, this type of notice has been successful in enhancing the research portfolio in other areas of special interest.

By fiscal year 1991, the initiatives described above will encourage a broad range of research and services research demonstration proposals. These efforts will develop a new cohort of scientists focusing on the mental health issues of rural populations. New investigators are anticipated to be recipients of FIRST awards and small grants. Other investigators are likely to propose services research demonstrations and possibly new research centers. High quality proposals will be supported within the research funding available to the Institute.

Overall, while NIH has supported a number of initiatives directed toward rural populations, there are still gaps in knowledge about the mental health concerns of rural groups, deficiencies in the availability of appropriate services for rural residents, and a lack of mental health professionals to provide services. Through its current work and by undertaking intensive new efforts, as described above, the Institute is addressing these challenges and working to improve rural mental health.

CENTERS FOR DISEASE CONTROL

RURAL HEALTH

Agricultural workers and their families experience a disproportionate share of injuries and diseases associated with numerous chemical, biological, and physical hazards.

In the FY 1990 budget, NIOSH was given $11,452,000 to expand activities in various specific ways for a national program to address the disease and injury problems in agriculture.

Using agricultural initiative resources appropriated by Congress for FY90, NIOSH is developing a coordinated program of surveillance, research and prevention activities. These include:

SURVEILLANCE

FARM FAMILY HEALTH AND HAZARD SURVEY: to determine to which hazards agricultural workers and their families are potentially exposed, the circumstances of exposures, and the health status of these workers and their families. This effort will be administered through cooperative agreements with the States, awarding 3-5 in FY 1990.

PUBLIC HEALTH NURSES IN RURAL COMMUNITES: nurses in 30 - 50 rural hospitals nationwide will: (1) work with County Extension agents and rural families to promote safety and health; (2) report agriculture-related disease and injury cases to the States and NIOSH; (3) provide safety and health instruction in high schools and vocational agriculture schools; (4) assist county and State Health Departments in surveillance and hazard evaluation.

INJURY SURVEILLANCE: (1) NIOSH is expanding the "Traumatic Injury Surveillance of Farmers" (TISF) project, which will be a mail survey, conducted in conjunction with land grant universities, to obtain national and State disability prevalence, injury incidence, and exposure information. (2) Complementing TISF, NIOSH and CEHIC, through NCHS in a special supplement to HIS, will obtain information to estimate total injuries, for workers and their family members, related to agricultural work.

RESEARCH

AGRICULTURAL CENTERS: Centers for agricultural safety and health will be established at sites across the country. They will conduct research, develop model educational programs, develop model prevention programs, assist and evaluate prevention programs implemented by the Agricultural Health Promotion System and others, devise and evaluate engineering and ergonomic technology, and provide consultation. In FY 1990, 2-4 Centers will be established.

LUNG DISEASE RESEARCH: in FY 1990, NIOSH will conduct laboratory and field research related to adverse respiratory effects from selected agricultural dusts.

In FY 1991 NIOSH will continue developing a coordinated program of surveillance, research, and prevention activities, by continuing the projects initiated in 1990.

The 1991 budget level of $11,329,000 reflects a decrease of $123,000 from the 1990 level. This is attributable to the non-recurring cost of the Surgeon General's Conference on Rural Safety and Health.

AGENCY FOR HEALTH CARE POLICY AND RESEARCH

Formerly the
National Center for Health Services Research
and Health Care Technology Assessment

RURAL HEALTH CARE

The Agency for Health Care Policy and Research (AHCPR) was established on December 19, 1989 as a separate Public Health Service (PHS) agency by the Omnibus Budget Reconciliation Act of 1989, P.L. 101-239. As authorized under a new Title IX of the PHS Act, the purpose of the agency is to enhance the quality, appropriateness, and effectiveness of health care services and to improve access to such services. This goal will be accomplished through the establishment of a broad base of scientific research and through the promotion of improvements in clinical practice and in the organization, financing, and delivery of health care services. The new agency replaces the former National Center for Health Services Research and Health Care Technology Assessment (NCHSR).

As the leader of Federal efforts in outcomes research and health services research, the AHCPR seeks to create and disseminate new knowledge and better understanding of the processes by which health services are made available and how they may be provided more efficiently and effectively. The AHCPR conducts and supports scientific research that tests the assumptions on which current health policies and practices are based, assesses the performance of the health care system, and examines alternate ways to organize, finance, and deliver health services. AHCPR's program is directed towards the needs of health care policymakers, providers, and consumers. It addresses the full array of health care issues, among them rural health care.

The former NCHSR was required by statute to undertake and support research, evaluation, and demonstration projects respecting the delivery of health care services in rural areas, including projects with respect to (1) the future of the rural hospital; (2) long-term health care for the rural elderly; (3) hospital care for the rural poor and uninsured; and (4) alternative health care delivery systems and managed health care in rural areas.

Rural health care will continue to be an area of special emphasis for the Agency for Health Care Policy and Research (AHCPR). In creating the new Agency, OBRA 1989 (P.L. 101-239) requires that, in carrying out the activities of Title IX of the PHS Act, AHCPR undertake and support research, demonstration projects, and evaluations with respect to the delivery of health care services in rural areas (including frontier areas).

Health services research on the delivery of health care services in rural areas is needed for many reasons. There are major differences in the organization and use of health care

resources between rural and urban areas. The number of physicians per capita, the number of hospitals and other institutional facilities per square mile, the extent of public control of health facilities, the travel time to obtain health care services and the use and complexity of health care services differ between rural and urban areas. The population served by rural hospitals also is different from that treated in urban hospitals. Rural hospital patients are older, are less likely to be on Medicaid or to be self-paying, and are admitted with diagnoses that require longer hospital stays on average. In addition to all of these difficulties, present economic conditions are having an effect the provision of adequate health care services to rural and frontier areas of this country.

In FY 1989-FY 1990, funds were appropriated to NCHSR (now AHCPR) to begin research on the rural health services research agenda developed during the FY 1987 conference on rural health issues.

Extramural Research

RURAL HEALTH CARE CONFERENCE

In FY 1987, the former NCHSR and HCFA awarded a grant to the National Rural Health Association, with co-sponsorship by the Foundation for Health Services Research, to convene a conference designed to [1] summarize key health care issues facing rural Americans; [2] identify gaps in current knowledge; and [3] formulate a research agenda to address these gaps.

An advisory committee, composed of rural health care research experts, providers, third party payors, health policy representatives and related government representatives designed the preliminary research agenda discussed at the conference and identified the conference participants. The conference brought together over 150 participants which included a mix of rural providers, rural health care professionals, policy makers, and health services researchers.

The research agenda addresses six issues of major concern to Federal, State and local policymakers--the rural hospital; alternative delivery systems and managed care; the poor and uninsured; maternal, child, and adolescent health care; the rural elderly; and primary health services.

The recommendations for rural hospital studies call for research on questions involving economic viability, the impact of Medicare's prospective payment system, hospital costs, quality of care, and diversification of services. Alternative delivery systems and managed care research topics include costs and utilization, quality of care, and questions specific to Medicare and Medicaid patients. Studies of the rural poor and uninsured

would examine uncompensated care, private health insurance and Medicaid coverage, health status, and access to care.

The agenda also calls for research aimed at building a basic data base about the health status and utilization patterns of rural children and the elderly, and to conduct small area analyses to provide information about the health problems of those groups. The sixth area of investigation--primary care, including emergency medical services--would examine the impact of diminished Federal support along with the effects of the rural economic recession; the relationship between health status and access to primary care; and other issues.

Further details, including a summary of the proceedings and copies of the background stimulus papers, are in "A Rural Health Services Research Agenda," a special February 1989 issue of Health Services Research.

To stimulate extramural research applications on rural health issues, a Program Note was issued entitled, "The Role of Market Forces in the Delivery of Health Care: Issues for Research." The Program Note identified several areas for investigator-initiated research on the costs and financing of rural health care as recommended by the 1987 Rural Health Care Conference participants. As a result of this Note, the projects described below were funded:

Projects Ongoing in Fiscal Year 1989:

"Rural Hospital Management Strategies and Viability"
Stephen Mick, Ph.D., University of Michigan (formerly of Johns Hopkins University), Grant No. HS05996

This study will examine the determinants, characteristics, and impacts of strategic management responses by rural hospitals to changes in their environment during the 1980s. The results of this study will provide knowledge about relationships between [1] changes in payment systems and local economic conditions during the 1980s and [2] rural hospital management strategies and economic performance. Evidence about the relative effectiveness of various management strategies may help rural hospitals adapt to their changing environment.

New Starts in Fiscal Year 1989:

"Health Services Impact of Community Health Centers (CHC) Use in Rural Maine"
Ronald Deprez, Ph.D., Medical Care Development, Inc., Grant No. HS05756

Rural Community Health Centers are private, nonprofit, fee-for-service health care organizations which provide

comprehensive services to residents of rural areas. Some of these centers are located in areas which qualify for Federal reimbursement of costs on the basis of need. Maine contains 32 CHCs, of which 18 rural CHCs receive Federal funds.

The objectives of this study are to examine the influence of provider, setting, and patient characteristics on hospital utilization in rural areas in Maine served by Community Health Centers (CHCs) and to assess the policy implications of those observations on Federal efforts to provide access to primary care in rural areas. Only the 18 Federally supported CHCs are included in this study.

The aims of this study are to determine (1) to what extent CHC use substitutes for hospital use, and for which population and diagnoses, after controlling for population and provider characteristics, (2) to what extent organizational and financing characterstics of primary care delivered in CHCs are responsible for the substitutive effect, (3) to what extent variation in hospital use is influenced by provider and/or practice compensation methods, and (4) how payment methods for physician and outpatient services in rural areas might be revised to achieve reduction in hospital use without sacrifice of quality of care by rural populations.

This research is a follow-up to a study conducted in 1984 by Medical Care Development (MCD) in which significant differences were observed in hospital utilization rates between users and nonusers of CHCs in rural Maine, suggesting a substitutive effect of CHC use for inpatient hospital care.

"Urban/Rural Differences in Elderly Use of Long-Term Care"
Dr. Charles McConnel, University of Texas Southwestern Medical Center, Grant No. HS06197

Dr. McConnel will establish the extent and determinants of differences in survival and utilization of health and community based services by the rural/urban elderly. Data from the Longitudinal Study of Aging, the Census of the Population, the National Death Index, and the Health Professionals Resource File will be linked. A single analysis will then link a defined population data by health status, health services access, and health services utilization. The outcome variables include: physician visits, nursing home admissions, home health and/or nursing visits, homemaker services, use of community services and hospitalization.

"Alternative Health Care Utilization in the Rural Elderly"
Dr. James Mitchell, East Carolina University, Grant No. HS05381

Dr. Mitchell will describe and model the use of alternative health care resources by rural poor and black

elderly. The variables which influence alternative care use will be identified. Seven hundred and ninety-eight rural poor and black will be identified in 10 of the 33 officially designated rural counties in North Carolina. All respondents identified in a personal interview as users of alternative care will again be interviewed in the home. The study will identify the reasons for alternative care by rural poor and black elderly and provide clues as to the dynamics of their health care utilization.

"Access to Medical Care Among the Indigent in Nebraska"
Dr. Keith Mueller, University of Nebraska, Grant No. HS05760

Dr. Mueller will identify the problems of access among the uninsured in rural areas and they will be compared to the difficulties in access to care for the medically indigent in urban areas. The number of medically indigent in Nebraska will be determined as well as their geographic distribution. This study will identify the changes in the number of uninsured in Nebraska since the recession and financial crisis in the agricultural economy in 1982-1983. Data will be collected through telephone surveys. Correlation analysis will be used to determine relationships between the dependent variables of income levels, county of residence, age, and occupation. Multiple regression analyses (including path) will be used to explain the incidence of medical indigence.

"Practice Variations in Prenatal and Intraparatum Care"
Roger A. Rosenblatt, M.D., University of Washington, Grant No. HS06166

This study will explore the relationship between variations in prenatal care received by low risk women in Washington state to provider type (obstetrician, family practitioner, nurse practitioner), location (urban/rural), practice organization and hospital setting. Outcomes to be collected include perinatal mortality, morbidity, and charges. The results will assist in decisions regarding appropriate utilization of prenatal technology for low risk women.

Intramural Research

The Agency's intramural research program also is examining issues relating to rural health care. The National Medical Expenditure Survey will provide a unique, updated data base for the analysis of how the population (including rural Americans) uses health care, what they pay for this care, and how expenditures are financed.

Another component of the intramural program, the Hospital Studies Program, is analyzing comparisons of rural hospitals with

their urban counterparts along a number of dimensions such as environment, service mix, and staffing patterns for all U.S. hospitals. Using about 400 hospitals within the Hospital Cost and Utilization Project (HCUP) sample, rural and urban hospitals are being compared in terms of case mix, financial position, and utilization of these institutions. Completed analyses using the second HCUP data base (containing summary abstracts of all patient discharges from the hospitals contained in the sample during 1980-1987) include: "Urban and Rural Hospital Costs: 1981-1985," and "Patterns of Travel for Rural Individuals Hospitalized in New York State: Relationships Between Distance, Destination, and Casemix." Future analyses using HCUP data include "Urban/Rural Differences in Hospital Labor Costs."

User Liaison Program

The User Liaison Program was established to convey relevant and timely health services research findings and related information to state and local government policymakers in a manner that allows such officials to absorb this information and thus heighten the possibility of research being employed in the decision making process. One of the Program's main functions is to identify pressing informational needs of state and local government officials that could be addressed by new health services research studies or by syntheses of existing research findings.

The issue of rural health care was the subject of a User Liaison Program workshop held in upper New York State in late FY 1989. This was the third rural health care workshop the User Liaison Program has conducted--earlier workshops being held in Oregon and Texas. Planning activities have taken place in FY 1990 with respect to another rural health care workshop which will be held in the South or mid-West later this fiscal year. Staff of the Office of Rural Health Policy in the Health Resources and Services Administration (HRSA) have been active participants in these efforts.

CENTERS FOR DISEASE CONTROL

RURAL HEALTH

Agricultural workers and their families experience a disproportionate share of injuries and diseases associated with numerous chemical, biological, and physical hazards.

In the FY 1990 budget, NIOSH was given $11,452,000 to expand activities in various specific ways for a national program to address the disease and injury problems in agriculture.

Using agricultural initiative resources appropriated by Congress for FY90, NIOSH is developing a coordinated program of surveillance, research and prevention activities. These include:

SURVEILLANCE

FARM FAMILY HEALTH AND HAZARD SURVEY: to determine to which hazards agricultural workers and their families are potentially exposed, the circumstances of exposures, and the health status of these workers and their families. This effort will be administered through cooperative agreements with the States, awarding 3-5 in FY 1990.

PUBLIC HEALTH NURSES IN RURAL COMMUNITES: nurses in 30 - 50 rural hospitals nationwide will: (1) work with County Extension agents and rural families to promote safety and health; (2) report agriculture-related disease and injury cases to the States and NIOSH; (3) provide safety and health instruction in high schools and vocational agriculture schools; (4) assist county and State Health Departments in surveillance and hazard evaluation.

INJURY SURVEILLANCE: (1) NIOSH is expanding the "Traumatic Injury Surveillance of Farmers" (TISF) project, which will be a mail survey, conducted in conjunction with land grant universities, to obtain national and State disability prevalence, injury incidence, and exposure information. (2) Complementing TISF, NIOSH and CEHIC, through NCHS in a special supplement to HIS, will obtain information to estimate total injuries, for workers and their family members, related to agricultural work.

RESEARCH

AGRICULTURAL CENTERS: Centers for agricultural safety and health will be established at sites across the country. They will conduct research, develop model educational programs, develop model prevention programs, assist and evaluate prevention programs implemented by the Agricultural Health Promotion System and others, devise and evaluate engineering and ergonomic technology, and provide consultation. In FY 1990, 2-4 Centers will be establshed.

LUNG DISEASE RESEARCH: in FY 1990, NIOSH will conduct laboratory and field research related to adverse respiratory effects from selected agricultural dusts.

In FY 1991 NIOSH will continue developing a coordinated program of surveillance, research, and prevention activities, by continuing the projects initiated in 1990.

The 1991 budget level of $13,029,000 reflects a decrease of $123,000 attributable to the non-recurring cost of the Surgeon General's Conference on Rural Safety and Health. The 1991 level also reflects an increase of $100,000 in other Farm Safety and Health.

Sexually Transmitted Diseases

Obligations

	1987 Actual	1988 Actual	1989 Actual	1990 Estimated	1991 Estimated
Public Health Service:					
Centers for Disease Control:.....	$59,942,000	$65,161,000	$78,700,000	$81,306,000	$81,420,000
National Institutes of Health:					
National Cancer Inst....	14,165,000	12,050,000	13,024,000	13,503,000	14,079,000
National Heart, Lung and Blood Institute.....	---	---	4,515,000	4,600,000	4,800,000
National Institute of Neurological Disorders and Stroke.....	194,000	206,000	225,000	232,000	243,000
National Institute of Allergy and Infectious Diseases.....	29,661,000	34,224,000	39,828,000	45,826,000	48,168,000
National Institute of Child Health and Human Development.....	5,502,000	6,424,000	5,642,000	5,900,000	6,100,000
National Institute of Dental Research.....	---	---	205,000	226,000	226,000
Division of Research Resources.....	1,398,000	570,000	738,000	568,000	505,000
National Center for Nursing Research.....	80,000	681,000	755,000	860,000	860,000
Office of the Director1/	---	78,000	---	---	---
Subtotal, NIH.....	51,000,000	54,233,000	64,932,000	71,715,000	74,981,000
Total	110,942,000	119,394,000	143,632,000	153,021,000	156,401,000

1/ Represents funds awarded through the ICDs for the Academic Research Enhancement Award Program

CENTERS FOR DISEASE CONTROL

Sexually Transmitted Disease

I. INTRODUCTION

FY 1989 was one of substantial activity in STD prevention and control. Prevention programs continued to expand; infectious syphilis substantially increased; congenital syphilis increased to the highest levels reported in nearly three decades; reported gonorrhea morbidity reversed its decade long decline; resistant gonoccocal infection steadily increased as a proportion of total gonorrhea; and ongoing studies indicate that Herpes simplex virus, type 2, has infected 30 million Americans.

Achieving the Year 1990 objectives to reduce morbidity and mortality from STD by preventing cases and complications requires a partnership effort and a sharing of responsibility by Federal, State and local governments, private medicine, and voluntary organizations. The Federal Government supports this partnership and meets its share of this responsibility through national leadership activities which include technical assistance in planning, developing and implementing control approaches; technical consultation in reviewing and monitoring control efforts; developing clinical standards and management systems; training; and providing epidemic assistance, disease information and prevention strategies. Direct Federal financial assistance is also a component of the partnership and supports disease monitoring, screening, sex partner notification services, STD health education, and other outreach efforts in all States. In addition, basic and applied research efforts are directed toward further characterizing the pathophysiology, host response, epidemiology, and behavioral aspects of these diseases to permit the development of improved diagnostic, prevention and control methodologies.

The major Federal foci for assistance to States are the Centers for Disease Control (CDC) and the HHS Regional Offices; and for research, are the CDC and the National Institutes of Health, including the National Institute of Allergy and Infectious Diseases (NIAID), the National Cancer Institute (NCI), and the National Institute for Child Health and Human Development (NICHD).

II. BACKGROUND

Preventing the spread of human immunodeficiency virus (HIV) and controlling the development of AIDS remains the Nation's number one public health priority. Since its transmission is primarily sexual, HIV has become the predominant STD. Currently, an estimated 1 million Americans are infected with HIV. In addition to HIV infection, STD, which threaten the health of primarily adolescent and young adult Americans each year, have increased to 12 million cases. Nationally, it is estimated that there are nearly 4 million chlamydial infections; 1.5 million cases of gonorrhea; about 110,000 new cases of syphilis; 1.2 million cases of nonchlamydial-nongonococcal urethritis; 1 million cases of nonchlamydial-nongonococcal mucopurulent cervicitis; 200,000 to 500,000 cases of genital herpes; 200,000 cases of Hepatitis B; 3 million cases of trichomoniasis; and 500,000 to 1 million cases of human papillomavirus infections. Over 750,000 cases of PID are diagnosed and treated each year resulting in approximately 210,000 hospitalizations (43 percent of these are younger than age 25 and 84 percent are younger than age 35), over 71,000 major surgical procedures (including over 29,000 hysterectomies), and over 88,000 ectopic pregnancies each year.

Women and children bear an inordinate share of the physical and emotional burden of STD. Prenatal STD also produces adverse effects on both pregnancy outcome and maternal/infant health, many of which are entirely preventable. Approximately 111,000 babies born each year will have chlamydial infection. For pregnant women with untreated syphilis, the risk of death of the infant is 40 percent, of delivery of an infant with congenital syphilis is 40 percent and of the delivery of a normal infant only 20 percent. As many as 3 of every 10,000 newborns are infected with herpes; more than 40 percent of those not treated will die within one year and half of the survivors will suffer serious and permanent mental damage. Congenital infection by cytomegalovirus (CMV) is estimated to occur in 1.5 percent of all pregnancies, and group B Streptococcus is estimated to cause symptomatic disease in 12,000 infants under 3 months of age annually and to cause nearly 5,000 infant deaths. NDTI analysis showed that first visits (an indicator of new cases) to private physicians for genital warts increased 9-fold from 1966-1988. Analyzed cervical cancer mortality trends which show that mortality rates have begun to increase among young women.

III. EFFECTIVENESS

Since the initiation of Federal assistance and efforts to control STD, reported cases of syphilis have declined 89 percent from an all-time high of 575,600 in 1943 to 110,500 in FY 1989. During this same period, first admissions to mental hospitals for syphilitic psychoses have declined by 98 percent and infant deaths caused by syphilis have declined 99 percent. However, infectious syphilis remained the number three reportable disease in FY 1989 and was exceeded only by gonorrhea and chicken pox. The reported

incidence of primary and secondary syphilis increased by 12.1 percent in FY 1989 and represents the highest number of reported cases in any year since 1948. All the increase has occurred in low-income, inner-city, heterosexual minority populations. Syphilis rates are 31 times higher among blacks and 11 times higher among hispanics than whites. Morbidity is also concentrated, with 63 percent of reported cases occurring in only 35 counties. Syphilis in white homosexual males has decreased since 1982 and remains at low levels. The increases experienced for the past three years have been associated with hard-to-reach foci of disease among "crack" cocaine users who are exchanging sex for drugs.

The rise in primary and secondary syphilis in heterosexual populations forewarned of congenital syphilis increases in future years. The magnitude of the increases, however, was completely unexpected. Reported congenital cases increased to 925 in FY 1989, reflecting a 37 percent increase over the 672 cases reported in FY 1988.

Gonorrhea continues to be the number one reportable communicable disease in the United States. Federally-assisted State and local gonorrhea control programs were implemented in FY 1982. Within one year, over 8 million women who were receiving pelvic examinations for other reasons were also screened for gonorrhea; this number has fluctuated between 5.3 and 8 million each year since then. From FY 1976 through FY 1981 the number of reported cases stabilized. Since 1981, cases of gonorrhea have decreased by over 34 percent despite social changes which placed increasing numbers of people at risk for STD. The declining trend that has been occurring over the last four years was reversed in FY 1989 when reported gonorrhea increased by 1.5 percent. Male cases increased by 3.2 percent and female cases increased by 1.5 percent. While some of this increase is artifact (the result of a case reporting procedures review and subsequent adjustment), it is also clear that a substantial portion is true increase. Intensive surveillance will be maintained to closely monitor these increases. The benefit-to-cost ratio of screening and outreach activities is estimated to be 2.9:1.

IV. PREVENTION AND CONTROL EFFORTS

The CDC provides active leadership and support for national efforts directed toward the control of STD to include: a national system to identify, investigate and monitor special disease control problems; the timely transfer of technological advances to improve State and local prevention and control programs; and applied research to develop new information about diagnosis, treatment, prevention and control of all STD.

Project grants awarded to State and local health departments and appropriate public and nonprofit entities emphasize the reduction of morbidity and mortality from STD through the development of prevention and control strategies and the implementation of nationally coordinated control programs focused on disease

intervention activities. The basic control program components are: (1) health promotion efforts directed toward people at risk to change high risk behaviors, prevent exposure and influence the infected to seek prompt medical care for themselves and their sex partners; (2) surveillance systems to monitor STD among specific populations; (3) surveillance and control activities directed toward antibiotic resistance; (4) hospital-based surveillance efforts for PID; (5) screening high-risk populations; (6) sex partner notification services for patients with gonorrhea, chlamydia, and infectious syphilis, (7) developing strategies for controlling STD and providing training for clinical skills improvement; and (8) involving the private medical community in all aspects of STD control.

In FY 1989, antimocrobial resistance remained a large and complex problem. Almost 53,000 cases of antibiotic resistant gonorrhea were reported, an increase of 62 percent over 1988. In a number of States, resistant strains have increased in prevalence to epidemic levels. More than 10 percent of all gonococcal resistance was reported from 5 states: Maryland, New Jersey, New York, Pennslyvania and Rhode Island. Nationwide, 7.0 percent of reported gonorrhea morbidity was caused by resistant strains in FY 1989. Because of this large proportion of resistance, the STD Treatment Guidelines were revised in September, 1989 so that ceftriaxone is now recommended for all cases of uncomplicated gonococcal infection.

Syphilis control efforts focus on disease-intervention activities including surveillance, case detection, and prevention, specifically of congenital syphilis. Follow-up of reactive serologic tests for syphilis resulted in the reporting of over 51,000 previously unknown/untreated cases of syphilis. During FY 1989, sex partner notification efforts were provided to individuals with infectious syphilis resulting in 19,800 new cases of syphilis being identified and treated and 45,900 exposed sex partners receiving preventive treatment. These screening and outreach efforts prevented an estimated 9,100 new cases of syphilis in fiscal year 1989. Clearly, however, these activities have fallen short of the ideal of control, i.e., continued reduction of morbidity in the population. One potential solution to this dilemma is to ensure that AIDS prevention activities also support syphilis control activities because of the association between genital ulcer disease and sexual HIV spread and the increases in syphilis occurring in populations already with a high prevalence of HIV infection secondary to illicit drug use.

National policy guidelines for the prevention and control of chlamydial infections were promulgated in 1985. Since then, STD control programs have made substantial advances in the development of prevention and control programs for chlamydia. Forty-two States have at least one city or county STD Control Program that offers comprehensive surveillance, diagnostic testing and treatment services, and 33 States also have laws or regulations requiring the reporting of chlamydia. Chlamydia control efforts implement a series of interventions similar to those used in gonorrhea control and include: use of erythromycin for eye prophylaxis in newborns to

prevent both gonococcal and chlamydial opthhalmia neonatorum; incorporation of information on the recognition and management of clinical syndromes caused by C. trachomatis into medical training programs; treatment of chlamydia infections which frequently coexist with gonococcal infections by employing a gonorrhea treatment regimen effective against both organisms; and using antichlamydial regimens for the treatment of sexual partners of patients who have clinical syndromes consistent with chlamydial infection.

Chlamydia intervention data reflect a two to threefold increase in testing activity in FY 1989 over FY 1988. During this period, 1.4 million women and 410,000 men were tested for chlamydia. Of these 197,000 (14 percent) women and 70,600 (17 percent) men were positive, with 94 percent (251,500) located and treated. Almost 61,000 patients were interviewed with over 47,000 sex partners referred for examination. Over 80,000 potential cases of chlamydia were prevented as a result of these activities. In FY 1989 approximately $18 million was devoted to this effort.

V. HEALTH PROMOTION

All sexually transmitted disease control project grants to State and local health departments include information and education activities as an integral portion of their control strategies. Control programs emphasize clinic based patient education/counseling designed to avoid future risk of infection and to improve health-seeking behaviors on the part of infected patients. Community education efforts are directed toward high-risk groups, such as pregnant females, homosexual men, adolescents, and intravenous drug users. Education efforts are also directed toward school-based populations, particularly in the implementation of effective HIV/STD curricula within the Nation's school systems. The effectiveness of health promotion activities varies. For example, homosexual males have apparently changed their high-risk behavior as morbidity for infectious syphilis and gonorrhea have decreased steadily among this population over the past three years. Unfortunately, the same messages delivered to the heterosexual core populations have not been as effective since infectious syphilis rates in his population have increased significantly in the past three years. Alternate health promotion approaches, including the direct funding of community-based organizations which represent and serve these populations, are being developed for this segment of the population.

Since 1979, CDC has provided partial support to the American Social Health Association to operate the National STD Hotline which provides STD information and referral services to almost 80,000

callers each year. Because of the Hotline's national visibility and importance, ASHA was awarded a contract for its operation in FY 1989 to increase the number of staff and telephone lines and reduce blocking rates.

VI. CLINICAL SERVICES/TRAINING

Adequate clinical management of patients and their partners is the final common pathway of STD control. Unfortunately, clinical services vary widely in different settings and are often inadequate to provide appropriate care for STD patients. The objectives of ideal clinical management are: 1) to determine the most likely etiology of the patient's complaint; 2) to provide appropriate treatment for that condition; 3) to detect other STD; 4) to ensure patient follow-up for test-of-cure after treatment; 5) to manage properly those patients who failed treatment; 6) to identify sexual partners for appropriate evaluation and treatment; and 7) to educate patients to reduce their risks of further disease acquisition. Thus, all key STD control strategies are contained in the microcosm of clinical services.

Since medical school curricula in the United States have not kept pace with the increasing incidence of STD, an integral part of STD control strategies has been to develop a coordinated system for training health care providers in this rapidly changing field. To this end, STD Prevention/Treatment Centers have been established at 11 sites. Each center is based on integration of a university medical school with a model public STD clinic for purposes of providing training for health care providers, and medical and nursing students. By FY 1989, almost 21,000 students had been cumulatively trained since 1979.

VII. RESEARCH

Both basic and applied research are crucial to STD control. Major changes in intervention strategy have accompanied the introduction of new antibiotics (e.g., penicillin), the development of better detection methods (e.g., Thayer-Martin media), the identification of resistant organisms (e.g., PPNG, CMRNG, TRNG), and the recognition of high-risk groups (e.g., homosexuals, patients with repeat infections, women with PID). Presently, quantum leaps in STD control programs await such developments as effective vaccines against HIV infection, herpes, or gonorrhea or more effective interventions with drug-using subcultures. Most STD research in the United States is supported by NIH and CDC, although an increasing amount is funded either by voluntary organizations concerned with the magnitude of the STD problem or by pharmaceutical firms or medical diagnostic companies aware of the potential market. The objectives of this research are to characterize the pathophysiology, host response, and epidemiology of STDs to allow further development of improved diagnosis, treatment, prevention and control strategies.

NIH supports a variety of basic science and clinical projects. These include development of gonococcal and herpes vaccines, experimental clinical trials with antiviral agents, determination of STD pathogens which predispose for HIV infection, establishment of herpes transmission patterns within communities, and determination of host responses to chlamydia infections. NIH also sponsors training of post-doctoral fellows in clinical and microbiologic STD research and has undertaken periodic workshops to update the most rapidly advancing areas of STD knowledge. The CDC, through the Division of STD/HIV Prevention (DSTD/HIVP) and the Division of Sexually Transmitted Disease Laboratory Research (STDLP), conducts applied research directed toward monitoring practical results and evaluating control strategies. This involves behavioral studies, clinical research, epidemiologic studies, and programmatic investigations.

VIII. PROGRAM ACCOMPLISHMENTS, FY 1989

A. Syphilis

- Directed congenital syphilis research on new serologic tests for diagnosis at birth.
- Simplified congenital syphilis protocol for determining which seropositive infants to evaluate and which infants to treat.
- Continued system for reporting unusual manifestations of syphilis in HIV-infected patients.
- Conducted eight outbreak investigations of syphilis.
- Continued study of natural history of syphilis in HIV-infected patients.
- Initiated a retrospective study of the natural history of syphilis among 710,000 patients treated at Staten Island.
- Identified and treated 51,000 (24 percent) of 217,200 persons with reactive tests for syphilis.
- Conducted sex partner notification activities that resulted in 19,800 new cases detected and almost 46,000 patients preventively treated.
- Conducted outreach efforts in syphilis control that resulted in the prevention of 9,100 new infections.

B. Gonorrhea

- Maintained 21 isolate monitoring laboratories to conduct surveillance of antibiotic resistance.
- Cultured 6.1 million women; of these, 264,400 (4.3 percent) were positive and 96 percent were located and treated.
- Examined 232,100 sex partners.
- Conducted outreach efforts in gonorrhea control that resulted in the prevention of 144,800 new infections.
- Conducted two outbreak investigations of resistant organisms.
- Continued diagnosis/treatment, epidemiology, and prevention/control research studies.

C. Chlamydial Infection

- Continued nationwide implementation of national policy guidelines for prevention and control of chlymadia.
- Developed a plan to initiate sentinel surveillance of chlamydial infections using an approach analogous to HIV Family Of Surveys.
- Continued risk factor study in family planning and prenatal clinics in Washington, Alaska, Oregon and Idaho.
- Began a comparison of inter-laboratory and inter-clinic variability of unsatisfactory samples for chlamydia testing.
- Continued a study at Emory University to evaluate the role of chlamydia infection on ectopic pregnancy.

D. Human Papillomavirus (HPV) Infection

- Continued ongoing collection system with a large commercial cytopathology laboratory to develop a surveillance system for cervical HPV infection.
- Continued research on the epidemiology of external genital wart infections.
- Continued study of the natural history of cervical HPV infection in Native American women.
- Continued a study of the natural history of cervical HPV infection in Detroit.
- Implemented study on multiple site HPV infection in Seattle.
- Implemented prevalence study of HPV in Alaska natives.

E. Herpes Simplex Virus Infection (HSV)

- Initiated study to determine the association of the presence of antibody to HSV-I and protection against infection with HSV-2.
- Completed a study to correlate HIV infection among patients with genital lesions.
- Completed a behavioral research study which shows that patients with genital lesions are less likely to use condoms and more likely to engage in anal intercourse.
- Continued cooperative studies to further define the epidemiology and natural history of HSV.
- Continued collaborative effort with FDA and pharmaceutical industry to monitor teratogenicity to acyclovir.

F. Other STD

- Continued to fill CDC's unique role of providing clinical, laboratory, and epidemiologic competence for chancroid, a disease of low but increasing incidence.
- Continued a case control study to determine risk factors for the acquisition of chancroid.
- Continued a study to characterize H. ducreyi strains

- Continued surveillance of metronidazole-resistance in T. vaginalis. In FY 1989, 16 States submitted resistant strains for testing; eighty-five percent of these isolates were resistant.

IX. PLANS FOR FY 1990

STD priorities are continually evolving because new STD are emerging as serious public health problems requiring innovative approaches to diagnostic, prevention, therapeutic, and case management services. The prevention and control of infectious and congenital syphilis, gonorrhea and chlamydia will continue to be major foci for control efforts in FY 1990. Because of the association between genital ulcer disease and sexual HIV spread and the increase of both syphilis and chancroid in populations already experiencing a high prevalence of HIV infection secondary to illicit drug use, it is crucial to again ensure in FY 1990 that HIV prevention activities both dovetail with and support genital ulcer disease control activities.

Education, the primary prevention tool available, will continue to focus on high-risk populations, particularly inner-city heterosexual minorities, STD patients, IV drug abusers, providers of medical care services, and the general public. Prevention/education efforts will also network with community based organizations representing groups at risk, especially minority groups, to use resources in the most efficient manner possible.

Interviewing/counselling of selected persons with STD will be provided, especially to young patients with their first STD infection, to patients with repeat infections, to patients with resistant gonococcal infections or other complications, and to those at high risk of acquiring HIV infection.

Technical assistance and consultation to State and local health departments will continue to emphasize improving diagnostic, clinical, and management techniques. HIV health education/risk reduction techniques will continue to be a focus of STD control programs.

Support will continue in major metropolitan areas for hospital-based programs to prevent and control pelvic inflammatory disease including infections caused by both gonorrhea and chlamydia.

The gonorrhea surveillance system to measure antibiotic resistance levels established at 21 laboratories will be continued.

Efforts to standardize, expand and upgrade the quality of data collection, analysis, interpretation and use at the Federal, State and local level will be continued. The microcomputer-based data network (MIS) will be further refined in all State and selected local health departments, with a statewide pilot microcomputer network being completed in California.

Training efforts in FY 1990 will focus on the further development of clinical experience in STD for students during their medical school and residency years. Existing STD Prevention/Training programs will be adjusted as new information or needs are identified and to ensure maintenance of the highest public health and clinical care standards.

STD management will emphasize additional skills in epidemiology to set priorities and provide the maximum yield per STD dollar invested.

Research to highlight the prevention of STD syndromes of greatest public health concern--infertility, ectopic pregnancy, pelvic inflammatory disease, and adverse reproductive outcomes--will be continued. Clinical trials of promising therapeutic alternatives for infections caused by resistant organisms will be continued. Studies to better define the problem of Chlamydia trachomatis and to seek public health applications of existing and new technologies will be continued. Studies will be continued to evaluate the toxicity and viral resistance of oral acyclovir for recurrent genital herpes. Finally, the CDC will also continue research to identify and reduce the incidence of unplanned infertility attributed to STDs.

National population-based research on the distribution of sexual behavior patterns across population sub groups will continued to be emphasized because of the priority of the incurable viral STD.

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases

SEXUALLY TRANSMITTED DISEASES

Each year in the United States, more than 13 million people acquire an infectious disease through sexual contact. This estimate does not include acquired immunodeficiency syndrome (AIDS). These sexually transmitted diseases (STDs) are responsible for immense physical and emotional suffering, with serious complications disproportionately affecting women. Pelvic inflammatory disease (PID), infertility, ectopic (tubal) pregnancy, cervical cancer, premature delivery, miscarriage, and neonatal death are among the most devastating consequences of STDs. The resulting financial burden on the health care system is estimated to exceed $3 billion annually.

NIAID's STD Branch, a part of the Division of Microbiology and Infectious Diseases, supports research aimed at preventing and treating STDs and their complications. Basic biomedical research is necessary for the development of vaccines and other preventive strategies. Equally important are clinical, epidemiologic, and behavioral research activities. The STD Branch places particular importance on basic studies directed toward developing vaccines for gonorrhea, chlamydial infection, and syphilis; animal and human studies of experimental vaccines for genital herpes; studies examining the pathogenesis (the development of disease), natural history, and therapy of human papillomavirus (HPV, the cause of genital warts); and studies of the mechanisms by which STDs result in adverse consequences during pregnancy. STD-related research is also supported by other branches of the Division of Microbiology and Infectious Diseases. The NIAID Division of Intramural Research conducts basic and clinical studies on a number of STDs, including genital herpes, gonorrhea, and chlamydial infection.

Other components of the National Institutes of Health that support research on STDs include the National Cancer Institute, the National Institute of Neurologic Disorders and Stroke, the National Institute of Child Health and Human Development, the National Eye Institute, the Division of Research Resources, the National Center for Nursing Research, and the Office of the Director.

Chlamydial Infections

Chlamydial infections are the most common bacterial STD in the United States today, affecting more than four million men and women each year. Infection with the bacterium *Chlamydia trachomatis* can cause nongonococcal urethritis (inflammation of the urethra, or urinary tube) in men; cervicitis (inflammation of the uterine cervix or lower portion of the womb) and salpingitis (inflammation of the

fallopian tube) in women; and proctitis (inflammation of the rectum) in both men and women.

Though readily treatable with antibiotics, chlamydial infections often go undiagnosed because early symptoms are usually mild or absent. Available diagnostic tests are expensive and therefore not routinely used. About 10 percent of untreated or inadequately treated chlamydial infections in women result in PID, infertility, or potentially life-threatening ectopic pregnancy (in which a fertilized egg implants in a fallopian tube instead of the uterus). PID caused by chlamydial infections is nearly three times as likely to lead to infertility as is PID caused by gonorrhea.

NIAID grantee Dr. Cho-Chou Kuo and his colleagues at the University of Washington, Seattle, used a monkey model to compare the natural course of primary and repeated chlamydial infections in tubal tissue. By grafting fallopian tube tissue under the abdominal skin of monkeys and injecting the tissue repeatedly with chlamydial bacteria, the researchers demonstrated differences in the particular types of immune cells, and the degree of tissue destruction and scarring following initial and recurrent infection. These findings provide evidence of a strong inflammatory response to repeated chlamydial infections and suggest that the tissue damage which leads to infertility or tubal pregnancy may be provoked by the body's own immune response rather than solely by the organism itself. Use of this animal model will enable scientists to study the effects of antibiotics, hormones, and substances that boost or diminish the immune response in the fallopian tube tissue. These studies may lead to insights about how to prevent infertility or other complications of chlamydial PID.

NIAID grantee Dr. Constance Rothermel of the Cornell University Medical College in New York City and her colleagues at the University of California, San Francisco, have been exploring how immune mechanisms may cause chronic inflammation and scarring following chlamydial infections. They studied the effects of the immune modulator interleukin-1 (IL-1), a substance produced by the body to turn on key parts of the immune system. The scientists performed a number of studies of cells in culture to determine whether chlamydia bacteria stimulate the production of IL-1. The investigators found that the organism is a powerful stimulator of IL-1 production and postulated that even very low levels of IL-1 produced over an extended period could have harmful consequences. Although IL-1 production helps tissues recover from an initial chlamydial infection, because it is an immune system stimulator, IL-1 may also play a role in the tissue damage and scarring that result after recovery has taken place.

A number of studies have reported an increased prevalence of chlamydial infection of the cervix among users of oral contraceptives. Scientists have been examining factors that promote the migration of chlamydial organisms into the upper genital tract

(uterus, ovaries, and fallopian tubes), which can result in PID. Dr. Almen Barron, NIAID grantee at the University of Arkansas for Medical Sciences, Little Rock, and his associates undertook a study of the effect of oral contraceptives on chlamydial infection of the genital tract. Using the guinea pig as a model, the investigators found that commonly used human oral contraceptives predominantly containing estrogen markedly altered the course of chlamydial infection of the upper genital tract. When inoculated with chlamydia bacteria, the animals given reproductive hormones developed infection in the uterus and the fallopian tubes, whereas in animals not given hormones, chlamydia generally did not spread into the upper genital tract.

The exact mechanism by which estrogen-dominant oral contraceptives enhance the course of chlamydial infection of the upper genital tract is not clear. However, a number of investigators have previously demonstrated that oral contraceptives delay production of IgG (the major antibody in the blood) and IgA (the major antibody in secretions). This delay may provide the chlamydial organisms with more time to reproduce and move up the genital tract unimpeded by protective antibodies.

Gonorrhea

Gonorrhea affects an estimated 2 million people in the United States each year; one-quarter of the reported cases are diagnosed in teenagers. Like chlamydial infection, untreated gonorrhea in women can lead to PID, infertility, or ectopic pregnancy. In recent years, in some parts of the United States, it has become increasingly difficult to treat gonorrhea effectively because the spread of antibiotic-resistant strains of *gonococcal bacteria (Neisseria gonorrhoeae)* has increased dramatically.

Research exploring the mechanisms through which gonoccccal bacteria develop antibiotic resistance is of high priority to NIAID. Dr. Ralph Judd, NIAID grantee at the University of Montana, Missoula, and Dr. Claude Garon, intramural scientist at NIAID's Rocky Mountain Laboratories in Hamilton, Montana, conducted studies aimed at furthering understanding of how gonococcal bacteria exchange genetic material. They demonstrated that, like some other kinds of bacteria, gonococci form pouches, called blebs, on the surfaces of their cell membranes. The investigators found that these gonococcal blebs contain intact and apparently functional genetic material. By forming bridges from one cell to another, blebs can transfer the genetic material from cell to cell. These findings suggest that penicillin resistance could be passed to another cell through the blebs on the cell surfaces and that bleb formation may play a role in the development of antibiotic-resistant gonococcal bacteria.

One of the most serious consequences of gonoccocal infection in women is the development of PID. A better understanding of the way

in which the bacteria damage the fallopian tubes may help scientists develop ways to prevent gonococcal PID. Dr. Zell McGee, NIAID grantee at the University of Utah School of Medicine, and his colleagues have demonstrated that gonococcal bacteria inflict damage on the cells lining the fallopian tubes both by direct action of the bacteria and through the production of toxic products. Using human fallopian tube cells in laboratory studies, they have shown that gonococcal bacteria attach to particular cells and stimulate the production of a chemical called tumor necrosis factor (TNF). The researchers found that TNF causes the death of special cells with hair-like appendages (called ciliated cells), which are essential for normal fallopian function. The loss of these cells is likely to interfere with the transport of an egg through the tube and may, therefore, result in ectopic pregnancy or infertility. This study suggests that antibiotic treatment of gonococcal PID may be more effective in preventing infertility if accompanied by agents that could block the production of or the effects of TNF. Future studies in animal models to confirm these findings will be necessary before clinical trials of such agents can be undertaken.

Genital Herpes

Each year in the United States as many as 500,000 people become infected with herpes simplex virus (HSV), the cause of genital herpes. Although two types of HSV can cause symptoms of genital herpes, HSV-2 most often affects the genital area, while HSV-1 usually affects the mouth and lips, causing cold sores and mouth ulcers. HSV-2 is often transmitted to others asymptomatically (when symptoms are absent). After initial infection, both types of HSV remain inactive in nerve cells and may reactivate periodically, with or without visible blisters or ulcers. Transmission of HSV from a pregnant woman to her developing fetus or to her baby during delivery can result in mental retardation or other neurological impairment, and other serious consequences for the baby. Like syphilis and other diseases that cause genital ulcers, genital herpes appears to play a role in the transmission of HIV, the cause of AIDS.

Researchers have had difficulty in estimating the number of individuals infected with HSV-2 because many do not experience recognizable symptoms. In addition, currently used blood tests are limited in their ability to distinguish HSV type 2 from HSV type 1 infection.

NIAID grantee Dr. Andre Nahmias of Emory University School of Medicine in Atlanta, Georgia, and his collaborators at the Centers for Disease Control were the first researchers to use a type-specific test for herpes in a large survey of the U.S. population. They used a newly developed test to detect the presence of antibodies to HSV-2 in blood samples from more than 4200 participants in the 1976-80 National Health and Nutrition Examination Survey (NHANES II).

Based on their findings, Dr. Nahmias and his colleagues estimated that at the time of the survey, 16 percent of the population over age 14 years of age--25.4 million Americans--was infected with HSV-2. Black women in particular were at high risk. Black men were about three times as likely as white men to have been infected with HSV-2, while black women were about six times as likely as white women to have been infected. Among blacks, women were more than twice as likely to be infected as men, while white men and women were equally likely to be infected. Because people at high risk for HSV-2 are also likely to be at increased risk for other STDs, including HIV infection, STD services and education programs are especially important for black women.

NIAID investigators are studying the effects of an experimental vaccine to prevent genital herpes infection. Dr. Stephen Straus and his coworkers in NIAID's Division of Intramural Research have initiated the first trial of an experimental vaccine derived from a genetically engineered protein of HSV-2. This study will determine the safety of the vaccine and the degree to which it stimulates the production of HSV-2 antibodies in the blood of both HSV-infected and non-infected individuals. Other vaccine candidates, such as live virus vaccines that are genetically modified to limit their ability to cause disease, are under study in animals and humans by NIAID-supported investigators.

In addition to its efforts to develop effective vaccines, NIAID conducts and supports research aimed at developing effective therapies for genital herpes. Dr. Straus has played a leading role in establishing the benefits of the antiviral drug acyclovir in preventing frequent recurrences of genital herpes symptoms. In a series of 5 studies, spanning 4 years, the investigators followed 47 healthy persons with frequent recurrences of genital herpes symptoms who were given daily oral acyclovir to suppress their outbreaks. Prolonged use of acyclovir was well tolerated, safe, and effective in suppressing genital herpes. Therapy was stopped after each 12-month interval during the study and resumed after a recurrence was documented.

Before entering the study, these patients had an average of 16 recurrences a year. During acyclovir treatment, only half of the patients experienced any recurrences. Most of these patients had a single recurrence, which was brief and mild. All patients had their typical pattern of recurrences shortly after therapy was stopped. However, about one-fifth of patients eventually discontinued therapy because their outbreaks took longer and longer to occur after treatment stopped, and they felt it was no longer necessary to continue taking acyclovir. The investigators observed that there was a gradual overall lessening of the disease over a period of years. Dr. Straus concluded that suppressive therapy should be terminated after one year but may be reinstituted if the time to

first recurrence after treatment stops suggests that the frequency of outbreaks remains high.

Reductions in recurrence rates may decrease the risk of acquiring HIV infection by decreasing the size and duration of herpes lesions, which may serve as a point of entry for HIV. In addition to the benefit in reducing recurrent outbreaks, the use of acyclovir may also lead to reduced transmission of genital herpes to uninfected partners.

Agents other than acyclovir are also being tested in NIAID-supported studies. NIAID grantee Dr. David Bernstein, of The James N. Gamble Institute of Medical Research in Cincinnati, Ohio, and Dr. Christopher Harrison, of Children's Hospital Research Foundation in Cincinnati, a grantee supported by the National Institute of Child Health and Human Development, have conducted studies in guinea pigs of an immune modulator called R837. An immune modulator acts directly on the cells of the immune system to produce or suppress production of chemicals that boost or reduce the body's immune response. R837 does not affect the reproduction of HSV-2 itself, but when administered topically once a day to lesions on infected guinea pigs, the compound was found to reduce symptoms, decrease viral replication, and reduce recurrent outbreaks of the disease by lowering the amount of virus latently infecting nerve cells. The next step in testing will be the study of topical R837 as a possible therapy for genital herpes in humans.

National Cancer Institute

This year, National Cancer Institute (NCI) scientists and grantees reported new findings on the association between human papillomaviruses and the development of cervical cancer and on human T-cell leukemia or lymphotropic virus types I and II.

Human Papillomaviruses

At least 60 different varieties of human papillomaviruses (HPV) have been identified. Some, like the ones that cause common warts, are not sexually transmitted and are not associated with cancer. However, about 20 types can be spread through sexual contact, and several of these are believed to play a major role in the development of cancer of the uterine cervix. An estimated 13,000 American women are diagnosed with cervical cancer each year, and 6,000 women die of the disease.

In a large, multicenter study, intramural scientist Drs. Louise Brinton, William Reeves at the Gorgas Memorial Laboratory in Panama, William Rawls at McMaster University in Ontario, Canada, and colleagues evaluated the relationship between infection with two strains of HPV (HPV-16 and HPV-18) and cervical cancer. Studying more than 2,200 women who live in four high-risk areas of Latin America, the researchers calculated that infection with HPV-16 or HPV-18 increased the risk for developing cervical cancer by as much as nine times. Risk persisted even after adjusting for other major risk factors, such as number of sexual partners. This is the largest case-control study conducted on HPV and cervical cancer, and the first to take into account other risk factors. The study was also funded by the National Cancer Institute of Canada.

In an effort to understand how viruses transform normal cells into cancerous ones, intramural researchers Drs. Peter Howley, Douglas Lowy, and colleagues have traced cellular transformation by HPV-16 and HPV-18 to two viral genes, known as E6 and E7. Intramural researchers Drs. Howley and Karl Munger, in collaboration with NCI grantees Drs. Ed Harlow and Nicholas Dyson at Cold Spring Harbor Laboratory in New York have discovered that the protein encoded by E7 can bind to another cellular protein, the product of the retinoblastoma (RB) gene, which normally inhibits cancer cell growth. By forming a complex with the RB protein, it appears that E7 allows normal cells to grow out of control. This finding has important implications in elucidating the mechanisms by which normal cells are converted to malignant ones.

6.

Pap Smear Reporting System

A new system to evaluate and report information from Pap smears, the most effective screening method to detect uterine cervical cancers, was developed by a group of cytopathologists and representatives of national medical and other organizations who convened for an NCI-sponsored workshop.

"The 1988 Bethesda System for Reporting Cervical/Vaginal Cytologic Diagnoses," or "The Bethesda System," replaces the Papanicolaou classification of Pap smears, which is now obsolete in modern cytopathology. The new system uses uniform diagnostic terms to describe what the cytotechnologist or cytopathologist sees in the Pap smear. It not only provides a clearer communication of diagnoses but also will facilitate quality control measures at laboratories where Pap smears are read. An estimated 15 to 40 percent of women who have cancerous or precancerous conditions have had inappropriately classified Pap smears, either because of laboratory error or because of clinician error in taking the samples.

NCI recommends that all women who are or have been sexually active, or who have reached the age of 18, have an annual Pap test and pelvic examination. After a woman has had three or more consecutive annual examinations with normal Pap test results, the test may be performed less frequently at the discretion of her physician.

Human T-Cell Leukemia or Lymphotropic Virus Types I and II

Human T-cell leukemia or lymphotropic virus types I and II (HTLV-I and -II) can be transmitted by blood, intimate sexual contact, in utero, or by breast milk. HTLV-I and -II are uncommon in the general U.S. population, but recent findings suggest the viruses may be more prevalent among intravenous drug users. HTLV-I causes a type of adult T-cell leukemia/lymphoma, certain B-cell leukemias (rarely), and a neurological disorder called HTLV-associated myelopathy. New findings suggest that the virus or a related virus detected by new technology also may be associated with some cases of multiple sclerosis. HTLV-II is associated with a more chronic form of T-cell malignancies than HTLV-I, but there are fewer studies of this.

Researchers are trying to determine the prevalence of HTLV-I and -II in the United States, but routinely used laboratory tests cannot distinguish between the two viruses. Studies indicate that intravenous (IV) drug users are at elevated risk of infection with HTLV-I and -II, although the risk varies across the country. It is not known how the viruses first entered this

population, but they are believed to have spread among IV drug users through the sharing of contaminated needles. There is a risk that infected individuals will spread the viruses to their sexual partners or that pregnant women may transmit the infection to their unborn babies.

New research suggests that HTLV-II, rather than HTLV-I, may be the more prevalent of the two viruses among IV drug users. NCI grantee Dr. Irvin Chen at the University of California at Los Angeles, Dr. Helen Lee at Abbott Laboratories in Chicago, Illinois, and colleagues found that 20 percent of IV drug users surveyed in New Orleans were infected with one of the two viruses. Applying a recently developed DNA sequencing technique that can distinguish between the two viruses, the investigators found that 23 of 25 individuals were infected with HTLV-II, and the other two individuals were infected with HTLV-I.

In support of these findings, intramural researcher Zaki Salahuddin with Dr. Robert Gallo and Drs. William Hall and Henry Kaplan at North Shore University Hospital in New York isolated HTLV-II from blood drawn from IV drug users and suggested that HTLV-II may be more prevalent than previously thought.

Intramural scientist Dr. Kenneth Cantor, Dr. Robert Battjes at the National Institute on Drug Abuse, and colleagues evaluated almost 2,000 IV drug users from across the United States for presence of HTLV-I or -II and found that 11 percent were infected. Their test could not distinguish between the two viruses, but the findings shed light on racial differences in infection rates. Twenty-one percent of blacks in the study were infected, 9 percent of Hispanics, and 5 percent of whites.

A study of stored blood samples has provided the best available indication of the prevalence of HTLV-I in the general U.S. population in the late 1970s, and the study will serve as a baseline for monitoring the spread of this virus. Intramural scientist Dr. Carl Saxinger, Robert Murphy of the National Center for Health Statistics, and colleagues reported HTLV-I infection in 20 of nearly 10,000 serum samples. A disproportionately high number of those persons infected were black. There was no apparent clustering of positive samples in any major geographic region or in either sex.

Some studies have suggested that in addition to HTLV-I's direct role in causing a type of adult T-cell leukemia/lymphoma, the virus may also play an indirect role in development of B-cell chronic lymphocytic leukemias. Intramural researchers Drs. Blattner and Dean Mann and colleagues found HTLV-I present in the T and B cells of patients in Jamaica who had B-cell

chronic lymphocytic leukemia. The findings suggest that HTLV-I infection of T cells may induce tumor development in B cells by some unknown mechanism(s).

Since November 1988, donated blood in the United States has been routinely screened for evidence of HTLV-I. Because of the difficulty in distinguishing between HTLV-I and -II in laboratory tests, it is expected that many units of HTLV-II-infected blood are also often eliminated in the screening process. Studying the risk of spread of HTLV-I/II by blood transfusion, intramural scientist Dr. William Blattner, Dr. Noah Cohen at Texas A & M University in College Station, Dr. Frank Polk at The Johns Hopkins University in Baltimore, Maryland, and colleagues found that the risk from screened blood is low in the United States. However, the risk was 10 times higher for transmission of HTLV-I/II than the AIDS virus. The transfusion-related risk for HTLV-I/II infection was 0.024 percent (five per 20,963 units). The study was funded in part by a contract from the National Heart, Lung, and Blood Institute.

National Institute of Child Health and Human Development

The National Institute of Child Health and Human Development (NICHD) supports research on the role of contraceptives in preventing the spread of STDs.

Last year, a major laboratory program designed to evaluate the suitability of using condoms and spermicides for STD prevention was completed. NICHD contractor Dr. Roger Detels at the University of California in Los Angeles conducted a condom testing program to determine if prophylactics purchased in stores meet industry standards for quality and are sufficient barriers against STDs. Roughly 1,000 of each of 31 different brands of condoms were tested for water leakage, pinholes, and elastic strength. The results testify that the high quality of the current supply of condoms on the American market should provide a substantial degree of protection against bacterial STDs that might serve as cofactors for acquiring AIDS.

Additional studies conducted at UCLA were designed to test the capability of condoms as shields against viruses. It was demonstrated that latex does not have holes or pores that would allow for the passage of viral particles of any size. Spermicides used in conjunction with condoms were found to provide additional protection against infection with STDs in the event of condom damage.

Also completed last year at UCLA was a spermicide testing program that compared the inhibitory effects of six spermicides on nine common STDs. All of the spermicides were effective against some of the STDs, although two formulas appeared to have the best overall effectiveness against a spectrum of disease agents.

NICHD grantee Dr. William Louv at the University of Alabama in Birmingham studied the relative risk of infections in spermicide users compared to nonusers. Results showed a 60 percent decline in the rate of gonorrheal infection and a 50 percent reduction in chlamydial infection in the spermicide users over a 6-month period. Rate reductions were less impressive in women who used spermicides on a sporadic basis.

National Eye Institute

Sexually transmitted diseases such as gonorrhea and chlamydial infection are major causes of neonatal eye infections, and infants who acquire these infections during birth have a high risk of developing conjunctivitis, an inflammation of the conjunctiva. To learn more about the risks and benefits of preventive treatment of neonatal conjunctivitis, the National Eye Institute (NEI) is supporting a study to assess the need for treatment and to evaluate various treatment alternatives.

The conjunctiva is a delicate membrane that lines the inside of the eyelids and covers the white part of the front of the eye. Since the conjunctiva passes over the cornea when the eyelids blink or close, conjunctivitis may also affect the cornea. If not treated promptly, conjunctival infections can lead to scarring of the cornea and blindness in these newborn infants.

More than a century ago, universal treatment of newborns to prevent conjunctivitis was initiated because of the high rate of gonococcal infection in the American population. Today, however, twice as many Americans develop genital chlamydial infections as gonococcal infections.

All 50 states still require some treatment to protect infants from eye infections at birth. For example, Washington state requires the administration of 1 percent silver nitrate drops or one of the antibiotic ointments, erythromycin or tetracycline. Some states, however, use only silver nitrate, which was the original treatment for gonococcal eye infections. Although it prevents gonococcal conjunctivitis, silver nitrate may also irritate eyes of newborns and cause chemical conjunctivitis. Consequently, many women who are at low risk for a sexually transmitted disease would prefer to have no preventive agent given to their newborns, although the law still requires it.

The medical literature does not clearly establish whether the risk to infants from no treatment is higher or lower than the risk from receiving a preventive agent. European countries without mandatory treatment of newborns' eyes do not seem to have a higher incidence of neonatal conjunctivitis than do countries that require treatment.

To evaluate the risks and benefits of treating all newborns to prevent these eye infections, the NEI is funding a randomized, controlled clinical trial of eye infection prophylaxis (preventive treatment) in the newborn. The infants are randomized to one of three groups: silver nitrate treatment, erythromycin treatment, or no treatment. Because some infants in the study are randomized to no treatment, the Washington State Board of Health has granted the investigators, led by NEI grantee Dr. Thomas Grayston at the University of Washington in Seattle, an exemption from the state law

requiring all infants to be treated prophylactically for neonatal eye infection. To protect newborns from potential gonococcal infection, all pregnant women and infants who test positive for gonorrhea are excluded from the study.

In addition to assessing the risks and benefits of no treatment, the study investigators are evaluating which drug is most effective for treating chlamydial infection, as well as less frequent neonatal eye infections, and the long-term effects of the treatment.

The 5-year study will include 800 infants born at the University of Washington Hospital in Seattle. Infants without conjunctivitis are monitored for 2 months after delivery. Infants with conjunctivitis at birth are monitored for 2 months after successful treatment of their infection. The investigators are continuing to recruit patients.

Division of Research Resources

DRR supports and conducts research into sexually transmitted diseases at shared research facilities across the United States. General Clinical Research Centers (GCRCs) provide the research infrastructure for multidisciplinary studies on both children and adults. Specifically, they provide patient research facilities, computerized data management and analysis, as well as research nurses, dietitians, biostatisticians, and specialized laboratories for the translation of basic and clinical research into medical practice.

Genital Herpes

One area of intense study by DRR-supported investigators is genital herpes infections. DRR grantees Drs. Charles Prober and Ann Arvin at the Stanford University GCRC in Stanford, California, have shown that most neonatal herpes infections are neither predictable nor preventable when the mother is asymptomatic. Therefore, physicians caring for newborns should consider the possibility of neonatal herpes when diagnosing sick infants during the first weeks of life, even when HSV infection of the mother is not apparent.

In this study, the investigators obtained specimens for viral cultures from mothers, infants, or both during 6,904 deliveries. HSV-2 was found in specimens from 14 women, all of whom were asymptomatic at the time of delivery. Only one had a history of genital herpes. Two of the 14 women had serologic evidence of a primary HSV infection at delivery. The child of one contracted neonatal herpes. None of the infants born to the 12 women who had serologic evidence of a previous infection with HSV-2 contracted the virus.

These findings, according to Dr. Prober, indicate that most infants at risk of exposure to HSV at delivery will not be identified if concern about asymptomatic shedding of virus during delivery is limited to women with a history of genital herpes infection.

Physicians should, therefore, concentrate on the much larger population of pregnant women who are unaware that they are infected with herpes. According to Dr. Prober, early attention to these women and their newborns could help reduce the morbidity and mortality associated with neonatal herpes infection.

Human Papillomaviruses

DRR grantees at the University of Alabama GCRC at Birmingham and investigators at other university medical centers are studying the effectiveness of two major classes of interferons, alpha and beta, genital warts, caused by certain types of human papillomaviruses (HPV).

Seventy-nine patients with genital warts resistant to conventional methods received three injections per week of one of the interferon types or placebo for 4 weeks. Injections were made directly into one wart on each patient. Forty-seven percent of warts treated with the interferons disappeared completely compared with only 22 percent of placebo-injected warts. Both types of interferons appeared equally effective in treating the warts. Administration of the interferons directly into the wart was nontoxic and well tolerated by the patients, although about one third of interferon-injected warts recurred after treatment stopped.

DRR grantee Dr. Richard C. Reichman at the University of Rochester in New York directs the multicollaborative study of which the University of Alabama in Birmingham is part. The research, supported primarily by the National Institute of Allergy and Infectious Diseases, is aimed at examining the role of interferons in treating genital warts. According to Dr. Reichman, these studies could lead to the first effective therapy for genital warts as well as methods for treating other types of HPV, which may cause genital tract cancers.

Previous research done at the University of Rochester GCRC under Dr. Reichman's direction found that parenterally administered interferon was effective in treating genital warts in 69 percent of subjects receiving low doses. Two additional groups of patients treated for genital warts with higher doses of interferon showed similar improvement.

Work at the collaborating centers is currently under way to determine optimum therapeutic regimens using different interferons administered parenterally in combination with conventional local therapy.

RESEARCH OUTLOOK

Today, in the face of evidence suggesting the role of STDs in HIV transmission and with the rising toll of AIDS mortality, the need for behavioral, epidemiologic, basic biomedical, and clinical research on STDs is greater than ever. The HIV epidemic has spurred scientific investigations aimed at finding new approaches to developing drugs, inexpensive and rapid diagnostic tests, and vaccines for STDs. Each step forward in treating, diagnosing, or preventing STDs will have an enormous impact on the quality of life for all segments of our population.

SPINAL CORD INJURY
Obligations

Public Health Service:	1987	1988	1989	Estimate 1990	Estimate 1991
National Institutes Health:					
National Institute of Neurological Disorders and Stroke	$29,816,000	$33,778,000	$36,036,000	$37,186,000	$38,898,000
National Institute on Aging	---	---	240,000	248,000	258,000
Division of Research Resources 1/	309,000	635,000	573,000	535,000	476,000
National Center for Nursing Research	298,000	118,000	282,000	320,000	320,000
Office of the Director, NIH 2/	53,000	56,000	---	---	---
TOTAL, NIH	30,472,000	34,587,000	37,131,000	38,289,000	39,952,000

1/ This includes RCMI awards. Prior to FY 1989, RCMI's were shown in OD.
2/ This includes AREA awards for FY 1987-1991, and RCMI awards for FY 1987-1988.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Disorders and Stroke

SPINAL CORD INJURY

Spinal cord injury resulting in paralysis is a devastating human health problem. It strikes our Nation's young people the hardest--two-thirds of all injuries occur in the under-30 age group. It disrupts family relationships and plans for education and marriage. Every year there are approximately 10,000 new injuries; and every year the cost of care and services for the estimated 250,000 to 500,000 survivors of spinal cord trauma increases, now exceeding $2 billion a year.

The time of greatest risk for injury is summer, when Americans spend the most time on the road, hiking and climbing, and swimming and diving. Although prompt emergency medical care saves the lives of many accident victims, survivors are often permanently disabled and face a lifetime of specialized care and rehabilitation.

The National Institute of Neurological Disorders and Stroke (NINDS) leads the Federal Government's research mission to overcome paralysis, and supports an extensive program of basic and clinical studies on the biomedical aspects of spinal cord injury. Major goals of this program are:

- To identify changes that take place in the spinal cord immediately after injury, and to find ways of preventing the damage these changes may cause;

- To understand the mechanisms of nerve growth and regeneration as a step toward reversal of paralysis and restitution of function; and

- To restore function by supplementing or bypassing damaged nerves through the use of electronic neural prostheses.

In addition to research support through its grant and contract programs, the NINDS supports a national program of Spinal Cord Injury Research Centers located at Yale University in New Haven, Connecticut; Ohio State University in Columbus; the Medical University of South Carolina in Charleston; and New York University in New York City.

Other Federal agencies oversee related programs on spinal cord injury. Other NIH components that are involved in biomedical research relating to spinal cord injury include the National Center for Nursing Research, which supports studies on nursing care for patients with paralyzing conditions; the National Institute on Aging, which supports research on the effect of

trauma on the elderly; and the Division of Research Resources, which develops and ensures the availability of a variety of resources necessary to the conduct of biomedical research at NIH-supported facilities. Within other parts of the Public Health Service, the Health Resources and Services Administration provides leadership in the delivery of health-care services to the injured; the National Center for Health Services Research studies the utilization and financing of such services; and the Center for Disease Control studies the prevention, acute care, rehabilitation, biomechanics, and epidemiology of all injuries, including those to the spinal cord. The National Institute on Disability and Rehabilitation Research, in the Department of Education, supports rehabilitation projects, and the Department of Veterans Affairs supports research to improve the quality of life of veterans with spinal cord injuries. Other Federal agencies that study various aspects of spinal cord injury include the Department of Defense and the Department of Transportation.

Controlling Secondary Damage

In the first few hours following injury to the spinal cord, the body reacts with a series of physiological changes, or secondary events, that may cause damage beyond that of the original trauma. Trauma causes the release of natural substances that influence edema (swelling), bleeding, ischemia (insufficient blood flow), inflammation, and pain. Some of these substances may actually contribute to subsequent secondary damage within the spinal cord, and ultimately to loss of function.

NINDS grantees are involved in laboratory studies of new drugs to expand the roster of pharmacologic agents that may control secondary damage following injury. Dr. Alan Faden at the University of California, San Francisco, reported that the experimental drug MK-801 lessened trauma-induced damage in rat nervous tissue, possibly by controlling calcium levels. Dr. Wise Young at New York University found that U74006F, an experimental synthetic steroid within a class of drugs called 21-aminosteroids, was more effective and caused fewer and less severe side effects than the previously tested, naturally occurring steroid methylprednisolone in controlling edema in rats.

In clinical work, Dr. Young and his associate, Dr. Paul Cooper, reported encouraging results using "plating," a surgical procedure to stabilize the spinal canal. Almost all patients with cervical spinal cord injuries entering the New York University Center during the past two years underwent immediate surgery during which a metal plate was screwed into vertebrae over the damaged segment of spinal cord. The research team found that most patients treated in this fashion could be moved within 24 hours of surgery, reducing the risk of pulmonary complications and bedsores. The surgery also eliminates the need for later

bone grafts or traction devices, and shortens the time spent in intensive care.

Rehabilitation Studies: Smoothing the Road to Recovery

NINDS grantee Dr. V. Reggie Edgerton and his colleagues at the University of California, Los Angeles, are studying aspects of recovery in adult cats with spinal cord injuries. They demonstrated that cats with such injuries can support their weight with their hind limbs while walking on a treadmill. While no hind limb training was necessary for the cats to walk at very slow speeds, such training did enhance the animals' ability to walk at faster speeds. Further, the investigators found that training such injured cats to stand stationary was actually detrimental to their regaining the ability to walk. Although it is not yet known whether this finding will apply to humans, it does raise important concerns for future clinical studies of spinal cord injury rehabilitation.

Care of injured patients extends well beyond the physical aspects of their condition. Dr. Gary Davidoff, an NINDS grantee at the University of Michigan at Ann Arbor, demonstrated that depression often goes unrecognized in people with spinal cord injury and is therefore left untreated. Untreated depression, Dr. Davidoff found, adversely affects a patient's adjustment to paralysis and motivation for rehabilitation.

Promoting New Growth in Damaged Nerves

Scientists know that damaged neurons in the central nervous system of laboratory animals are able to regrow. Achieving the same results in the damaged human spinal cord, and getting the neurons to resume transmitting signals, are the ultimate goals of nervous system regeneration studies. A major drive is under way to understand the bodily mechanisms that control and encourage nerve growth, a key element in restoring function to paralyzed humans.

One area of study focuses on nerve growth factors, natural substances that initiate and support new cell development, guide new or damaged nerves to appropriate targets, and assist in the maintenance of neuronal function. An intriguing nervous system component associated with growing nerve processes is a protein called GAP-43. Several NINDS-supported scientists are exploring the potentials of this nerve growth factor.

Dr. Larry Benowitz and colleagues at McLean Hospital in Boston, Massachusetts, located the human GAP-43 gene on chromosome 3 and established the protein's amino acid sequence, an important step toward understanding GAP-43's role in the human nervous system. The research team also mapped the distribution of GAP-43 in the human brain. Dr. Benowitz reported the abundant

expression of the protein in the associative area of the neocortex, which is involved in learning, and lesser amounts in other brain regions. This suggests an interrelationship between learning, memory, and neuronal growth. The continued growth and rearrangement of nerve connections may be particularly necessary in these regions. Finding GAP-43 in abundance in the human central nervous system indicates its importance to neuronal growth, and imparts a new relevance to GAP-43 animal studies.

Working with rat tissue, Dr. John A. Freeman at Vanderbilt University in Nashville, Tennessee, found evidence that GAP-43 may act to regulate levels of calcium within growing nerves. That finding was reinforced in work by Dr. Pate Skene at Stanford University in California, who confirmed the role of the GAP-43 molecule in controlling calcium entry into rat nerve cells. Dr. Skene suggests that insertion of GAP-43 DNA into injured neurons may be a way to initiate a regenerative response, and he has recently embarked on work to test his theory.

Regenerating neurons need some kind of supporting structure, or substrate, on which to grow. Such a substrate should also direct the growing nerves to appropriate targets, allowing them to make connections that will transmit signals from one neuron to the next. A promising area of research focuses on natural and synthetic materials that may support and enhance regrowth of nerve cells and axons.

In a joint laboratory study at the University of California, San Diego, NINDS grantees Drs. Marston Manthorpe and Silvio Varon isolated a substance from human amniotic membrane that promotes nerve growth. (Amniotic membrane has been used successfully as substrate material.) Dr. Manthorpe has determined the amino acid sequence of this substance (called hAMM), a first step toward developing a synthetic form of the material.

Dr. Patrick Aebischer, an NINDS grantee at Brown University in Providence, Rhode Island, is studying how various types of synthetic guidance channels affect regeneration in the peripheral nervous system of mice. Such channels have been considered inert conduits providing guidance to sprouting nerve axons and preventing the invasion of scar tissue. More recent studies have shown that the channels play a more active role in the regeneration of injured nerve cells. Dr. Aebischer has found that permeability and electrical properties of the channels can influence peripheral nervous system regeneration in mice. Permeable channels help regulate the movement of nutrients and growth factors, which affect the growth of nerve axons. Channels made of electrically charged materials also enhance peripheral nerve regeneration.

Growth of nerve cells and axons is but one part of the regenerative process. The growing axons need a protective

covering, known as the myelin sheath, in order to transmit signals. To learn how to encourage remyelination of injured axons in the central nervous system, scientists are studying the peripheral nervous system, which has the innate ability to repair itself.

Schwann cells, which surround the axons of peripheral nerves, are responsible for myelination of those axons and may be key elements in peripheral nerve regeneration. By implanting pure Schwann cells, NINDS grantee Dr. Mary Bunge and her colleagues at Washington University in St. Louis, Missouri and the University of Miami in Florida, achieved extensive remyelination of central nervous system axons in newborn rats with a genetic myelin deficiency. This work proved that peripheral nerve cells could survive and function appropriately when implanted into the central nervous system. Dr. Bunge will expand her work on the Schwann cell's possible role in the repair and remyelination of spinal cord axons after traumatic injury.

Several NINDS-supported laboratories are exploring the use of implants of animal fetal nervous tissue to improve function in areas of the spinal cord damaged by trauma. Dr. John Houle, at the University of Arkansas in Little Rock, and Dr. Paul Reier, at the University of Florida in Gainesville, showed that implants of rat fetal spinal cord survived for extended periods when placed into the injured rat spinal cord. Such implants appeared to prevent or reduce scarring at the injury site, long believed to be an impediment to regeneration.

By transplanting fetal rat spinal cord into both newborn and adult rats with spinal lesions, Dr. Reier and NINDS grantee Dr. Barbara S. Bregman at Georgetown University in Washington D.C., were able to promote survival of some damaged neurons. The investigators suggest that it is possible that the region of the graft served as a favorable environment through which spinal neurons could project. Or, the transplanted fetal tissue might itself be developing circuitry similar to that normally seen in the spinal cord.

Dr. Bregman has also implanted several different kinds of embryonic cells into rats with spinal cord lesions. All implants survived and, in the short term, were able to support the temporary survival of neurons. In the long term, however, only implants of embryonic spinal cord supported the survival of the injured cells. It may be that both environmental factors (such as nourishment from any implanted tissue) and mechanical factors (the terrain on which cells grow) are necessary for the growth of cells in spinal cord injury.

Neural Prostheses: Bypassing the Damage

The NINDS Neural Prosthesis Program supports and encourages research on the development of implantable devices to compensate electronically for lost sensory and motor functions.

One such device, developed by NINDS contractors Drs. Hunter Peckham, J. Thomas Mortimer, and others at Case Western Reserve University in Cleveland, Ohio, has recently moved out of the laboratory and into the clinical arena. This device restores an elementary form of hand grasp to quadriplegic patients who retain some ability to move their shoulders. The device uses implanted electrodes driven by signals from a microcomputer cued to perform its functions by changes in the angle of the shoulder opposite the affected hand. Several movements can be accomplished with this device including opening, closing and locking in place. Two clinical centers in Canada are evaluating the system.

Other scientists are testing implant materials for safety and effectiveness. Under an NINDS contract, Dr. Lois Robblee and others at EIC Corporation in Boston, Massachusetts, developed and patented an electrode coated with iridium oxide that can deliver more signal per unit area than conventional materials like platinum or stainless steel. Extremely small electrodes capable of stimulating discrete groups of nerve cells can now be produced, thus greatly increasing the degree of control exerted by implanted electronic devices.

Iridium oxide coating is also being used by Dr. Ken Wise, an NINDS contractor at the University of Michigan in Ann Arbor, who has developed an electrode probe with 5 stimulating sites. The next generation of this probe will have 16 stimulating sites on a shaft about the thickness of a human hair.

At the Huntington Research Institute in Pasadena, California, NINDS contractor Dr. William Agnew, after demonstrating that nerve degeneration in cat tissue could be produced by continued high frequency electrical stimulation, has established safe limits for electric currents used in implantable neural prostheses. He found that when damage occurs, it is caused by excessive neural activity, and not by a toxic effect of the implanted electrodes or electrical current. Dr. Agnew and his colleagues have developed both implantable and penetrating electrodes that stimulate neurons more selectively than earlier models. The investigators are continuing tests to determine how much stimulation is needed to produce the desired effect without causing damage to the affected nerves.

Research Outlook

Results from Federally supported research have strengthened the hope that therapies to heal and repair the injured spinal

cord can and will be achieved. To augment this new knowledge, NIH will continue to stimulate and encourage innovative work in both the laboratory and the clinic to hasten the injured patient's physical and psychological recovery. The NINDS continues to support research training to develop the next generation of neuroscientists, who may one day realize the final triumph over spinal cord injury and paralysis.

CENTERS FOR DISEASE CONTROL

National Center for Health Statistics

SPINAL CORD INJURY

There were an estimated 16,000 patients hospitalized in short-stay hospitals in 1987 who had a first-listed diagnosis of spinal cord injury. About 75 percent of these patients were in the 15-44 year age group and 75 percent were males. The average length of stay for both sexes was 24.8 days. In addition to the 16,000 first-listed diagnoses of spinal cord injury, there were an additional 14,000 secondary diagnoses of spinal injury. Due to the fairly high relative standard error associated with such a low number of discharges, care should be taken in comparing the age and sex ratios to the 1986 data.

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STROKE
Obligations

Public Health Service:	1987	1988	1989	Estimate 1990	Estimate 1991
National Institutes of Health:					
National Institute of Neurological Disorders and Stroke.....	$41,728,000	$41,477,000	$44,928,000	$46,362,000	$48,496,000
National Heart, Lung and Blood Institute...	11,236,000	11,675,000	11,875,000	12,200,000	12,700,000
National Institute on Aging.....	361,000	---	855,000	885,000	920,000
National Institute on Deafness and Other Communication Disorders.....	---	---	2,895,000	3,611,000	3,772,000
National Center for Nursing Research.....	54,000	65,000	293,000	330,000	330,000
Office of the Director, NIH 1/.....	---	70,000	---	---	---
TOTAL, NIH.....	53,379,000	53,287,000	60,846,000	63,388,000	66,218,000

1/ Represents funds awarded through BIDs for Academic Research Enhancement Awards.

NATIONAL INSTITUTES OF HEALTH

National Institute of Neurological Disorders and Stroke

STROKE

Stroke, the Nation's third leading killer, affects nearly 400,000 Americans each year, with almost 150,000 dying from stroke-related causes. Although the stroke mortality rate continues to fall, the stroke incidence rate is increasing. Nearly 2 million stroke survivors may endure crippling disabilities, including paralysis, loss of speech, and lapses of memory.

Black Americans experience a higher incidence of stroke than white Americans. According to the National Center for Health Statistics, black men aged 35 to 75 years are 2.5 and black women are 2.4 times as likely to die of a stroke as their white counterparts. Survival rate following a stroke is poorer for blacks than whites.

The effects of a stroke are devastating, but there is hope for these millions through the research efforts of the National Institute of Neurological Disorders and Stroke (NINDS), which serves as the focal point for the Federal Government's biomedical research effort to discover what causes stroke and to develop more effective methods for prevention, treatment, and rehabilitation.

The NINDS program supports a broad spectrum of studies by investigators across the country. Scientists at Institute-sponsored research centers focus on stroke to further understand this debilitating disease. The national stroke research program of the NINDS is further strengthened by the efforts of the National Heart, Lung, and Blood Institute (NHLBI), which concentrates its studies on cardiovascular stroke risk factors like high blood pressure and atherosclerosis (narrowing of the arteries due to buildup of fatty substances). Also complementing NINDS research efforts are those of the National Center for Nursing Research (NCNR) which supports studies on methods to control hypertension in individuals at risk for stroke. NCNR scientists are developing and testing techniques to improve the care and rehabilitation of patients who are incapacitated as a result of stroke. Research efforts on stroke are also supported by the National Institute on Deafness and Other Communication Disorders, the Division of Research Resources, and the Office of the Director, National Institutes of Health.

Evidence that this stroke research effort is yielding results is the steady decline in the national stroke death rate, a remarkable 27 percent drop over the past decade:

Year	No. of Fatal Strokes	Rate per 100,000
1977	181,934	84.1
1979	169,488	77.0
1981	163,504	71.3
1983	155,598	66.5
1985	151,810	64.1
1987	149,835	61.6
1988	150,300 (provisional)	61.1

This decline in the death rate has been attributed both to heightened public awareness of the dangers of high blood pressure and other factors that increase stroke risk, including transient ischemic attacks (TIA's or small strokes), cardiac diseases, and diabetes, and to major advances in treatment during the acute stroke period.

In spite of the decline in deaths, stroke remains a public health problem of great magnitude. The incidence of stroke is again increasing and still presents the challenge of developing better preventive, diagnostic, and treatment methods. Studies conducted by NINDS grantees Dr. Jack Whisnant of the Mayo Clinic and Foundation in Rochester, Minnesota, and Dr. Philip Wolf of the Boston University School of Medicine in Massachusetts, have shown that decline in stroke mortality is not necessarily correlated with a decline in stroke incidence. In fact, Dr. Wolf's evaluation of data from the Framingham Heart Study demonstrates increases in stroke incidence. With the aging of our population comes the potential for even greater stroke incidence.

What Is A Stroke?

A stroke is usually the culmination of progressive disease that may have developed over many years but is only rarely detected early in the disease process in a routine physical examination. In some cases, stroke takes people completely by surprise. Many attacks, however, can be prevented by heeding warning signs and the risk factors identified through stroke research. TIA's, for example, are "little strokes" that warn that a major stroke may be imminent. Symptoms of TIA may include tingling or weakness in a limb or on one side of the face, loss of strength in a limb, difficulty with speech, or temporary blindness in one or both eyes. Although these symptoms disappear within 24 hours, and often within minutes, they represent a medical emergency and require immediate evaluation and treatment.

Stroke occurs when there is a sudden loss of brain function caused by decreased blood flow to a part of the brain. Some strokes have little recognizable effect. Others can quickly cause death. Most strokes are triggered by one of the following events: (1) thrombosis, when a blood clot forms within a blood

vessel of the brain or neck; (2) **cerebral embolism**, when a blood vessel in the brain is blocked by a clot carried through the circulation from some other part of the body, often from the neck blood vessels or heart; (3) **stenosis**, when an artery supplying blood to the brain becomes severely narrowed, usually as a result of atherosclerosis; or (4) **cerebral hemorrhage**, when a cerebral blood vessel ruptures, with bleeding into brain tissue or into the spaces surrounding the brain. The term "ischemia," often used in connection with stroke, describes the condition of reduced blood flow to an area of the brain that leads to tissue damage in that area.

Most strokes happen when a blood vessel in the brain becomes blocked by a clot or partially obstructed by stenosis. Neither type of blockage is generally fatal but in those stroke cases that do result in death, 75 percent are due to blood vessel blockage. The second greatest cause of stroke deaths is cerebral hemorrhage, which occurs less often but accounts for about 15 percent of the fatalities.

Factors that Foretell Stroke

Predicting a stroke before it strikes could save many from suffering the incapacitating effects of this disease. NINDS-supported scientists are looking at the various risk factors that may indicate that a stroke will happen or recur. Much of their research is built upon increased understanding of the unique mechanisms that control cerebral blood circulation and brain metabolism.

Glucose levels, as well as blood viscosity or fluidity, may indicate an individual's risk of stroke. NINDS grantee Dr. De Courten-Myers at the University of Cincinnati in Ohio found that the extent of damage in experimental stroke was much greater when blood glucose levels were elevated. This finding could have important implications in the treatment of patients by controlling glucose levels at the time of a stroke. Furthermore, Dr. Bruce Coull, an Institute grantee at the Oregon Health Sciences University in Portland, analyzed the glucose levels of more than 350 individuals: those with recurrent stroke and TIA compared with persons who had experienced a single stroke or who were at risk but had never had a stroke. His analysis revealed that persons who are not diabetic but have blood sugar levels higher than normal may be at higher risk for having a stroke. Dr. Coull had found previously that patients with thicker than normal whole blood or plasma (high viscosity) are also at increased risk.

Blood sugar levels are also implicated in stroke in a study by Dr. Carlos Kase, an NINDS grantee at the Boston University School of Medicine. He examined the brain scans of patients in the Framingham Heart Study who experienced strokes. Dr. Kase found that an inability to metabolize glucose normally was

especially prevalent in patients experiencing "silent strokes;" i.e., strokes without major symptoms. Careful control of blood sugar levels may be indicated in such patients.

Another stroke risk factor under investigation is atrial fibrillation, a type of irregular heartbeat that occurs in a large segment of the older population and produces a 5- to 10-fold increase in stroke risk. An NINDS-funded multicenter clinical trial under the direction of Drs. Robert Hart and David Sherman at the University of Texas in San Antonio, is attempting to determine whether aspirin or warfarin--drugs that will stop platelet activation and slow blood clotting, respectively--will significantly reduce stroke in people with atrial fibrillation without causing additional complications.

Until recently, a partially blocked carotid artery--the major supplier of blood to the brain--was often considered an indicator of impaired cerebral circulation that would put a patient at risk for stroke. Arterial surgery was frequently advised to remove obstructive deposits. Investigators at Washington University in St. Louis, Missouri, led by Institute grantee Dr. William Powers, conducted a two-part study using blood pressure and flow measurements obtained by positron emission tomography (PET) scanning to predict stroke risk in patients with a narrowed carotid artery but no evidence of stroke. From the initial study, Dr. Powers and his colleagues concluded that such PET-obtained blood pressure and flow measurements may not be good predictors of higher risk for early stroke.

Treatment Possibilities Under Investigation

Cerebrovascular clinical research centers and program projects are key components of the NINDS stroke research program. Institute-funded scientists at these centers strive to understand what causes a stroke and what the implications are for improved methods of treatment. There are 14 such centers, located at some of the nation's leading biomedical institutions: Duke University in Durham, North Carolina; Washington University in St. Louis, Missouri; the Mayo Medical School; The Johns Hopkins University in Baltimore, Maryland; the University of Maryland in Baltimore; Cornell University Medical College in New York City; the University of Pennsylvania in Philadelphia; Bowman Gray School of Medicine at Wake Forest University in Winston-Salem, North Carolina; Massachusetts General Hospital in Boston; the Oregon Health Sciences University in Portland; the University of Texas in Houston; the University of Iowa in Iowa City, Iowa; the University of Miami in Miami, Florida; and Henry Ford Hospital in Detroit, Michigan.

These clinical research centers also serve as a research training ground for young scientists and physicians in the areas

of neuroscience, neurosurgery, language disorders, and other fields related to the function of the brain.

NINDS grantee Dr. Myron Ginsberg at the University of Miami center is studying rats to determine if selective brain cooling can avert the injurious effects of a stroke. He found that brain temperature was critical in determining whether damage-causing defects in the blood-brain barrier occurred as a result of a transient ischemic period. Indications of injury were seen if brain temperature was elevated. Conversely, lowering brain temperature when blood was recirculated back into the brain following transient ischemia appeared to have a protective effect within a specific area of the brain. This study holds promise for future treatment in humans.

Scientists are investigating ways to alter the chain of events leading to the development of blood clots--thrombi and emboli, the causes of many strokes. Platelets, the smallest cell components in the blood involved in clotting, are the focal points of a number of studies. Dr. Kenneth Wu at the University of Texas has identified the receptor on platelets and is examining its interaction with clotting factors. This work may help prevent stroke by blocking the binding of platelets and hindering clot formation.

Atherosclerotic plaques were analyzed by Institute grantee Dr. Mark Fisher at the University of Southern California in Los Angeles. His experiments suggest that blood platelets participate in atherosclerotic plaque formation without necessarily forming a thrombus. This implies that platelets in the plaque may contribute in previously unknown ways to the formation of deadly obstructions in the arteries. Therefore, currently available drugs directed at platelet activity may be unable to prevent entirely the sequence of events resulting in such obstructions.

Limiting the damage brain cells sustain during a stroke could reduce the amount of disability a person suffers. NINDS grantee Dr. Blaine White at Wayne State University in Detroit, Michigan, is developing molecular tools to detect brain DNA that is harmed by a biochemical reaction that occurs when oxygen is restored to the brain following a stroke. If such DNA damage is found to occur in humans, specific therapeutic agents to reduce the damage could rescue critically ill brain cells from death.

With Institute support, Dr. Richard Kraig at the University of Chicago, has measured the alkalinity and acidity (pH) of specific brain cells during and following ischemia because the pH (acid-base) environment of brain cells is key to their survival. He found that an enzyme, astroglial sodium/potassium ATPase, which helps to maintain pH may also influence blood flow in the brain. Since this enzyme has implications for cellular survival

Dr. Kraig's work may be important in regulating edema formation associated with stroke and the brain damage caused by swelling. The toll of cellular death could be limited if the appropriate pH levels were restored to the injured area.

Many scientists believe that there may be a "window of opportunity" during which cells that have been damaged by ischemia may be salvaged. In another study, NINDS grantee Dr. Roger Simon at the University of California, San Francisco, has documented the time course of altered metabolism in the region of the rat brain where nerve cell death was experimentally induced. Dr. Simon observed changes in brain metabolism that may be suppressed by medication within the time frame necessary to keep the brain viable.

Restoration of blood flow to injured nerve cells at risk for death is the ultimate aim of work conducted by NINDS grantee Dr. Michael Moskowitz at Massachusetts General Hospital. Dr. Moskowitz has demonstrated that blood flow changes in the cortex are controlled by reflex-like mechanisms in the brain. These natural mechanisms are activated during emergencies like a stroke to control the force of blood surging through the brain. If scientists could learn how to manipulate these mechanisms, the damage done to the brain by excess blood flow and edema could be minimized.

Stroke patients recovering from language dysfunction or aphasia may benefit from the research of Drs. Marcus Raichle and Steven Peterson, NINDS grantees at the Washington University School of Medicine who are using PET to learn about the neurological basis of language. They discovered that the processing of language is much more complex than previously believed because several components of the brain operate simultaneously to produce words. Since stroke patients with aphasia have lost their ability to speak or to understand language, this finding may be the basis for developing new methods to help restore their language capabilities.

Tissue plasminogen activator (tPA), a drug that dissolves blood clots, is being evaluated in stroke patients to determine its safety; tPA may cause serious brain hemorrhaging if administered in an improper dose or at the wrong time. Dr. John Marler of the NINDS Division of Stroke and Trauma is the project director of this study. Over 50 patients have been enrolled in the participating institutions: Cornell University Medical Center in New York City, the University of Cincinnati in Ohio, and the University of Virginia, Charlottesville. Initial results of this study indicate that early stroke treatment with tPA shows promise. A larger clinical trial is planned with 280 patients to establish whether there is a direct link between patient improvement and administration of the drug.

Evaluating Surgery to Prevent Stroke

The unfortunately high incidence of stroke provides investigators with large populations of patients to study. NINDS-supported investigations that monitor these populations over many years offer unusual opportunities to evaluate the long-term effects of stroke damage and the effectiveness of treatments.

Eighteen medical centers are participating in an NINDS-funded 5-year clinical trial of carotid endarterectomy, a widely used surgical procedure aimed at preventing stroke by removing fatty blockages from the carotid artery in the neck. The study will involve some 1,500 patients with asymptomatic narrowing of the carotid artery. All will receive aspirin, a common preventive treatment for stroke, and the best possible medical care currently available. Half of the patients will also undergo carotid endarterectomy.

The trial began in the fall of 1987 under the direction of principal investigator Dr. James Toole at Wake Forest University in Winston-Salem, North Carolina. It is designed to answer two important questions:

o Does endarterectomy and optimal medical treatment in asymptomatic patients reduce the incidence of TIA and stroke significantly more than optimal medical treatment alone does?

o If it does, is this reduction sufficient to justify the possible surgical complications of the operation?

A second multicenter 5-year study of carotid endarterectomy funded by NINDS is being directed by Dr. Henry J.M. Barnett at the University of Western Ontario in Canada. This study focuses on patients who have already experienced a TIA and are therefore at increased risk of stroke to determine if these symptomatic patients are likely to benefit from carotid endarterectomy for stroke prevention. Half of the patients are selected at random to undergo carotid endarterectomy. All patients are receiving optimal medical care that includes antihypertensive treatment for those with high blood pressure and counseling about diet and smoking.

Stroke: Why Does It Affect More Minorities?

Two NINDS-supported studies are under way to elucidate the disparity of stroke incidence and mortality between black and white Americans. Dr. Ralph Sacco of Columbia University in New York City is initiating the first 5 year study of what prompts stroke recurrence in blacks and Hispanics. Dr. Sacco is enrolling patients in his study, and will be evaluating risk factors such as family history of stroke, diet, blood glucose and

cholesterol levels, and smoking to determine which factors may be responsible for causing another stroke.

At the University of Maryland in Baltimore, Dr. Steven Kittner is in the third year of a 5-year epidemiological investigation to answer such questions as: 1) What is the incidence of different types of stroke in blacks compared to whites? 2) If significant black-white differences in specific types of stroke incidence exist, are they explainable by different rates of hypertension and diabetes? and 3) Is there evidence to suggest that hypertension or diabetes is a more potent risk factor for stroke among blacks than whites? Thus far, preliminary findings show that neither hypertension itself nor differences in compliance with drug treatment and medical care related to hypertension or diabetes contribute to increased stroke risk among blacks. Both the Columbia University and University of Maryland studies should shed light on the factors responsible for causing stroke, and it is hoped, result in improved prevention strategies applicable to both blacks and whites.

National Heart, Lung, and Blood Institute

The National Heart, Lung, and Blood Institute (NHLBI) supports research related to cardiovascular disorders and risk factors that can result in stroke. Hypertension, a major risk factor for stroke and a major focus of NHLBI-supported research, is the topic of a separate report.

Framingham Heart Study Cohort Studied for Impact of Smoking on Stroke Incidence

The impact of cigarette smoking on stroke incidence was assessed in a cohort of the Framingham Heart Study, through a contract with Boston University. Regardless of smoking status, and in each sex, hypertensive individuals had twice the incidence of stroke. However, smoking was significantly related to stroke after age and hypertension were taken into account. Even after the results were controlled for pertinent cardiovascular disease risk factors, cigarette smoking continued to make a significant independent contribution to the risk of stroke generally and brain infarction specifically. The risk of stroke increased as the number of cigarettes smoked per day increased. The risk of stroke in heavy smokers (more than 40 cigarettes per day) was twice that of light smokers (fewer than ten cigarettes per day). Former smokers developed stroke at the same level as smokers soon after they had stopped smoking, but the risk of stroke decreased significantly by 2 years and was at the level of nonsmokers by 5 years after smoking cessation.

Relationship Between Stroke and Physical Disability Examined

The Framingham investigators examined the amount of residual disability attributable to stroke among 2,540 community-dwelling stroke survivors, 27 years after their initial examination. They examined the relationship between stroke and physical disability after controlling for age, cardiovascular risk factors, other cardiovascular diseases, and eight general health conditions related to physical disability. Among men living in the community, a history of stroke explained 12 percent of physical disability. Among women, however, stroke was not as strongly related to physical disability, accounting for only 3 percent. These results sugggest that although older men and women die from the same major causes, they may not be disabled by the same conditions.

Studies Focus on Regulation of Blood Flow to Brain

The area postrema is a region in the brain that plays an important role in the control of the cardiovascular system. It may function as a sensor for vasoactive substances, such as angiotensin and vasopressin, that are involved in the normal control of blood pressure and the breakdown of this control in

hypertension. Dr. Donald D. Heistad, a grantee at the University of Iowa, Iowa City, has developed a method to study, for the first time, the microcirculation of the area postrema in an animal model. Already, fundamental differences have been discovered between the blood vessels of this area and those elsewhere in the brain. In the area postrema, the lining of the blood vessels allows substances to pass from the blood vessels to the surrounding brain stem, quite unlike vessels in most other areas of the brain, where a "blood-brain barrier" exists. This leads to the speculation that the area postrema may be more sensitive to circulating stimuli and its blood vessels may function differently than those with impermeable linings. Studies such as these, which examine the regulation of blood flow to the cerebral hemispheres, the brain stem, and the surface of the brain are important in coming to understand how hypertension affects brain blood vessels and predisposes an individual to stroke.

Dr. Gary L. Baumbach, a grantee at the University of Iowa College of Medicine, Iowa City, has used stroke-prone spontaneously hypertensive (SHRSP) rats and normal Wistar-Kyoto (WKY) rats in a precise examination of the structure of small arterioles on the surface of the brain, in an attempt to quantify differences. By measuring volume density and cross-sectional area, and combining these data with biochemical analyses of the vessel walls, Dr. Baumbach has shown that the stiffness of arterioles in the SHRSP rat is reduced, rather than increased as might be expected, in comparison with those of the WKY rat. This reduction in stiffness is associated with excessive growth of the vessels, which have increased amounts of smooth muscle and elastin (a pliable component of the wall). The finding that blood vessels in the brain of hypertensive stroke-prone animals have increased distensibility opens up new possibilities for research on the role of the mechanics of these vessels in the development of stroke.

Dr. John R. Crouse, a grantee at the Bowman Gray School of Medicine, Winston-Salem, North Carolina, is using B-mode ultrasonography to study the nature and extent of arteriosclerosis of the carotid arteries in patients. The carotid arteries supply blood to the brain, and may become narrowed by arteriosclerosis. The extent of this narrowing may be measured by B-mode scanning, a noninvasive technique in which a television monitor displays images of the artery wall based on echoes of ultrasound directed to the target by the investigator. Dr. Crouse has demonstrated that B-mode can quantify the amount of progressive narrowing of carotid arteries in individual patients as arteriosclerosis progresses. Furthermore, progression of carotid arteriosclerosis has been shown to be more pronounced in patients with coronary heart disease, compared to coronary disease-free controls. These findings lay the groundwork for studies of risk factors for progression of carotid

arteriosclerosis, and may make possible calculations for interventions designed to retard this progression. The technique used by Dr. Crouse may allow early identification of individuals likely to develop such cerebrovascular events as transient ischemic attacks and stroke.

National Institute on Deafness and Other Communication Disorders

The National Institute on Deafness and Other Communication Disorders (NIDCD) conducts and supports research and training on disorders of hearing, balance, voice, speech, language, taste, touch, and smell.

Aphasia Research Emphasizes Brain Lesions, Organization

Aphasia, often seen in adults who have suffered a stroke, can also result from a brain tumor, infection, or a head injury. Aphasia is the loss of the ability to make sense of or use language, and includes the inability to understand the printed word.

NIDCD-supported investigations of aphasia associated with stroke include those carried out at the Boston University Aphasia Research Center. Dr. Harold Goodglass is conducting a series of studies focusing on clinical, psycholinguistic, and cognitive aspects of aphasia. For example, CT scans of 135 aphasic patients are being examined to document the relation of lesion to particular aphasia patterns and recovery from aphasia. Other studies are comparing verbal expression and language understanding in aphasics.

Dr. Edgar Zurif, also at Boston University, is investigating how communicative capacities are organized in the brain to arrive at neurologically interpretable analyses of such capabilities. Scientists are hopeful that this research will yield a more complete picture of communicative capacity in aphasic patients and provide a basis for remedial treatment.

Research Outlook

Stroke incidence is on the rise, and cerebrovascular disease continues to be a major cause of death and disability. As the population ages, there are more people at risk for stroke. Improved methods of diagnosis as well as greater physician and public awareness have increased the likelihood of detection.

While modifying lifestyle--not smoking, eating healthy foods, and recognizing stroke's warning signs--may save lives, it is imperative that research continue. Scientists are learning more about the complex mechanisms of stroke damage, and how to intervene. Promising drugs, along with traditional surgical treatments, have come under the scrutiny of clinical trials. Finally, prospective and retrospective epidemiological studies are helping to further define the profile of populations at risk for stroke.

In the 1990's--the Decade of the Brain--research on stroke treatment and prevention efforts will likely save and improve more lives than ever before.

CENTERS FOR DISEASE CONTROL

National Center for Health Statistics

STROKE

Based on the 1988 data from the National Hospital Discharge Survey, there were an estimated 784,000 discharges from short-stay hospitals in the United States with a first-listed, or principal, diagnosis of cerebrovascular disease (stroke). These patients, with a first-listed diagnosis of stroke, remained in the hospital for an average of 9.7 days. This means that over 7.5 million days of patient care were required for those patients having a first-listed diagnosis of stroke. Approximately seven out of every ten patients (74 percent) with a first-listed diagnosis of stroke were at least 65 years of age; however, the proportions of men and women were 57 percent women and 43 percent men.

1988, the National Health Interview Survey collected data on the prevalence of cerebrovascular disease for the civilian noninstitutionalized population of the United States. The number of persons who reported ever having cerebrovascular disease (including stroke) and surviving was 2,516,000 a rate of 10.4 per 1,000 persons. Of the age groups, those 65+ reported the highest rate, 50.1 per 1,000 persons. In this age group, persons over 75 had a rate of 66.8 per 1,000 persons. Females and males reported a similar rate of stroke: 9.9 and 11.0 respectively for females and males per 1,000 persons. These estimates only partially reflect the extent of this disease, however, since the fatality rates from it are high.

Information from the National Vital Statistics System indicates that cerebrovascular diseases were the third leading cause of death in the United States in 1987, accounting for 149,835 deaths or 7.1 percent of all deaths in that year. Since 1950, the death rate from this cause has declined steadily. The risk of death from this cause is 16 percent higher for males than for females and 82 percent higher for the black than for the white population.

PUBLIC HEALTH SERVICE AND GOVERNMENT-WIDE

SUBSTANCE ABUSE

Budget Authority/Obligations

HHS	1987 Actual	1988 Actual	1989 Actual	1990 Estimate	1991 Estimate
ADAMHA	$736,978,000	$740,341,000	$1,119,320,000	$1,833,661,000	$2,019,219,000
HRSA	134,000	465,770	304,906	318,000	--
IHS	49,409,000	45,535,000	49,859,000	65,839,000	67,880,000
CDC	--	15,000,000	20,000,000	25,000,000	30,197,000
FDA	1,600,000	1,600,000	7,000,000	7,200,000	7,400,000
FSA	--	--	3,000,000	995,000	--
HDS	--	--	30,000,000	29,602,000	35,602,000
Total HHS	788,121,000	802,941,770	1,229,483,906	1,962,615,000	2,160,298,000
Office of National Drug Control Policy	--	--	3,500,000	37,000,000	66,500,000
Special Forfeiture Fund	--	--	--	109,000,000	128,000,000
DOL	5,800,000	3,100,000	38,600,000	71,600,000	87,500,000
DOEd	200,000,000	229,800,000	376,300,000	562,500,000	617,700,000
USDA	4,300,000	6,500,000	6,500,000	6,700,000	17,600,000
DOD	496,200,000	200,600,000	501,600,000	877,600,000	1,207,800,000
VA	82,800,000	88,500,000	242,000,000	271,400,000	300,000,000
Justice	1,268,700,000	1,436,500,000	2,470,600,000	3,789,100,000	3,824,800,000
Treasury	515,700,000	484,500,000	702,500,000	806,500,000	778,900,000
Transportation	551,000,000	520,200,000	643,000,000	703,500,000	772,600,000
State	127,500,000	114,100,000	141,800,000	295,600,000	528,400,000
Interior	15,000,000	9,600,000	13,400,000	29,500,000	38,900,000
ACTION	7,800,000	5,900,000	10,100,000	9,200,000	9,600,000
White House Conference	5,000,000	2,500,000	--	--	--
HUD	--	--	8,200,000	98,400,000	150,000,000
US Courts	N/A	N/A	208,800,000	324,500,000	403,200,000
Total, Substance Abuse	4,067,921,000	3,904,741,770	6,596,383,906	9,954,715,000	11,091,798,000

ALCOHOL, DRUG ABUSE AND MENTAL HEALTH ADMINISTRATION

National Institute on Drug Abuse

INTRODUCTION

Drug abuse research is a diverse area of scientific inquiry, with activities ranging from basic studies of molecular mechanisms to applied studies of drug abuse in the workplace. Thus, research supported by the National Institute on Drug Abuse includes studies on the nature and extent of drug abuse, the biological, behavioral, and social contributors to drug abuse, the adverse consequences of drug abuse, the treatment and prevention of drug abuse, and the spread of HIV infection associated with drug abuse. NIDA also supports research training of new investigators and the career development of established researchers in both basic and clinical research related to drug abuse. Collectively, these activities constitute part of the national effort to reduce the demand for illicit drugs.

Drug abuse has waxed and waned as a health and social problem in the United States since the mid-19th century. The 1960's marked the beginning of the most recent upsurge in drug abuse, a period in which the percentage of people aged 14 to 25 in our population began to swell as the "baby boomers" came of age. Many middle class values were rejected by young people; and the use of drugs, especially marijuana, became a symbol for the counter culture. Retrospective surveys showed that in 1962, four percent of young adults aged 18-25 had tried marijuana. By 1967, 13 percent of young adults had tried marijuana, but by 1979, the number rose to 68 percent. In some areas, the use of marijuana came to be viewed almost as a rite of passage for youth. This period between 1967 and 1979 signaled a major departure from the previous pattern of drug use: drug use had breached the confines of the poor communities and had become prevalent in a large segment of our society, including the middle class, the mainstream of America, and in particular, its youth.

Extent of Drug Abuse: Knowledge about the extent of the problem comes from national surveys of household residents and high school seniors, and surveys of other selected populations. While overall prevalence has declined since the early 1980s, drug abuse continues to be a major public health problem. According to present estimates, one-third of all Americans 12 years of age and older have used an illicit drug or used drugs non medically at some point in their lives, and more than one-half of American youth have experimented with illicit drugs before finishing high school. The most commonly used illicit drugs in the U.S. are marijuana and cocaine. The use of smoked cocaine or "crack" has increased dramatically over the past five years. At present, new admissions to drug treatment programs most commonly report cocaine as their primary drug. Cocaine is also the illicit drug that causes the greatest number of hospital emergency room visits.

Research has identified a number of behavioral, biomedical, and neurobiological factors that are involved in drug abuse.

Behavioral Research: The role of abused drugs as behavioral reinforcers is evidenced by their inherent ability to establish and maintain the behavior that leads to their administration, i.e. abused drugs are said to have functional properties similar to food, water, and sex. This concept of reinforcement has strenghtened our understanding of the nature of drug dependence, has made possible animal behavioral studies of drug dependence, and has provided new methods of screening drugs for abuse potential. The development of animal methods for screening new drugs for abuse potential has kept several drugs with abuse potential and without unique medical properties from being marketed.

Biomedical Research: Biomedical research has resulted in the discovery of the receptor sites where abused drugs act in the central nervous system. Opiate receptors and subsequently endogenous peptides (endorphins and enkephalins) were discovered in the mid-1970s by drug abuse researchers. These peptides, normally present in the body, activate the opiate receptor to produce opiate-like effects. At present, a number of opiate receptors and opioid peptides have been identified. While research in this area has implications for many areas of medicine, in drug abuse this basic research is expected to lead to the development of new treatment medications.

Neurobiology: In neurobiological research, evidence exists that the behavior reinforcing effects of abused drugs are due to effects of the drugs on the brain's reward system. This neural network is responsible for the subjective experience of pleasure. Research has identified dopamine-containing neurons of the ventral tegmental area (VTA) as one of the neurochemical systems involved in the mediation of the drug reinforcement effect. Neurobiological research also has differentiated brain sites involved in behavioral reinforcement from those involved in physiological dependence.

Adverse Consequences of Drug Abuse

Use of illicit drugs has adverse consequences for both the individual and society. These include:

Crime: Various studies have shown that heroin addicts commit an average of 178-375 crimes per year while addicted. The most typical crimes involve drug sales, prostitution, procuring, gambling, and alcohol violations. Current estimates place the cost of drug-related crime in the U.S. at $20 billion/year. A recent study found that 75 percent of all arrestees in a sample from 14 urban areas tested positive on urinalysis for recent illicit drug use.

Pregnancy: Research has found that opiate-addicted women show increased rates of preterm deliveries and spontaneous abortions. In addition, their children are often born opiate-dependent and show respiratory problems and increased birth defects. Marijuana use by pregnant women is associated with low birth weight in their children, and possible neurodevelopmental impairment. Just how extensively exposure to in utero cocaine affects neonatal neurodevelopment is not yet known, but animal studies show that cocaine administered during pregnancy can impair learning and memory in the offspring.

Neurotoxicity: Research is finding that at least some of the residual disturbances in behavior, mood, and memory associated with drug abuse are a function of neurotoxicity (killing of nerve cells). Evidence exists (in either humans or animals) that neurotoxicity may be caused by a wide range of abused drugs, including solvent inhalants, amphetamines, certain meperidine analog "designer drugs" (when contaminated with MPTP), certain hallucinogenic amphetamines (MDA, MDMA or "Ecstasy"), and marijuana. Research is now geared to determining the mechanisms of neurotoxicity so that effective treatments can be developed.

Psychiatric Disorders: Psychiatric disorders are often associated with drug abuse and may represent a consequence of illicit drug use. Depressive symptomatology is commonly seen in opiate addicts on admission to treatment, paranoia characterizes chronic stimulant abusers, and psychosis is associated with PCP abuse. Research has found that drug abuse treatment often resolves these psychiatric conditions. In certain cases, however, psychiatric disorders persist after entry into treatment and require treatment in their own right. Since psychiatric symptomatology is predictive of poor treatment outcome, the finding that drug abusers entering treatment today have more disturbed psychological profiles than similar patients a decade ago, is of great concern.

Decline in Productivity: Research has shown that drug abuse in the workplace contributes to increased absenteeism, job turnover, accidents and injuries, and health care costs. Since research has developed sensitive and accurate procedures for detecting illicit drug use, monitoring is now possible. Interventions have been designed and studies are currently assessing the effectiveness of these interventions for reducing and eliminating illicit drug use in these applied settings.

AIDS: The spread of AIDS is certainly associated with IV drug users, but other drug abusers are at risk as well: those who exchange sex for crack, and others who because of drug use have impaired immune systems. The sexual partners of drug abusers and infants born to at risk women are also in peril.

Other Diseases: AIDS is not the only disease to afflict drug abusers. Hepatitis and HTLV I (a cousin to the AIDS virus, HIV) are very common viral infections in drug abusers. Pneumonias and

other diseases associated with poor nutrition and poor grooming habits also abound.

Accident and Death: According to NIDA's Drug Abuse Warning Network (DAWN), the number of people admitted to emergency rooms following cocaine use increased over five-fold from 1984 to 1988. Furthermore, the number of people who died following cocaine use more than doubled during the same time period. From 1984 to 1988 emergency room visits increased by nearly 1.5 times for heroin use, and by 2.3 times for marijuana use. —

Risk Factors in Drug Abuse

Not everyone uses illicit drugs and not everyone using illicit drugs becomes drug dependent. Risk factors are influences that contribute to an individual's tendency to use illicit drugs and to become drug dependent. A major area of drug abuse research is, therefore, identification of risk factors for drug abuse.

Behavioral and Psychosocial Factors: Research has identified childhood and adolescent behavior that predicts later drug abuse and has found that early use of certain drugs serves as a "stepping stone" for later use of other, more dangerous drugs. One of the most important findings in this area has been the role of peer influences on adolescent drug use. Counteracting this influence to use illicit drugs has been the focus of several successful drug abuse prevention programs, such as "Just Say No." Also known to contribute to drug abuse are environmental factors, including drug availability and consequences associated with illicit drug use.

Biological/Genetic Factors: Genetic factors are known to elevate risk for the development of alcoholism, and now evidence is pointing toward a role for genetic factors in drug abuse as well. For instance, animals have been bred that show a preference for self-administration of abused drugs; and human adoption studies have found that drug abuse in adoptees is associated with alcoholism and antisocial personality in their biological parents. Genetic factors may strongly influence the physiology of a drug response, as well. For example, rate of drug metabolism, affinity of the receptor for a drug, rate of neurotransmitter turnover, degree of neuron autoregulation, etc. could be inherently determined.

Psychiatric Factors: Not only may psychiatric disorders be the consequence of drug abuse, but they may be the cause of drug abuse as well. Research has consistently shown that early antisocial personality disorder is associated with later development of opiate addiction. In addition, individuals with a major depressive episode or anxiety disorder were found to have twice the risk for later developing drug abuse as individuals without these psychiatric disorders.

Treatment and Prevention of Drug Abuse

Knowledge derived from studies of basic mechanisms, adverse consequences, and risk factors in drug abuse provides the foundation for research efforts geared to improving the effectiveness of prevention and treatment strategies.

Prevention: In preventing drug abuse, peer education programs have been found to be the most effective in increasing knowledge and negative attitudes about illicit drug use, and thereby decreasing the onset of illicit drug use. From an analysis of national trend data, researchers have reported that declining use of marijuana by high school seniors can be directly linked to perceptions of adverse effects and social disapproval that is associated with the use of illicit drugs. Research has found that prevention programs which provide alternatives to drug abuse (e.g., wilderness training, personal competence development) are also effective in preventing illicit drug use.

Treatment Outcome: In treatment, both psychosocial interventions and medications have been evaluated and were found to be effective in reducing illicit drug use. In addition, both types of treatments have been found to be effective in reducing criminal activity and in increasing employment and psychological functioning. Pretreatment level of drug use, criminal activity, and psychiatric symptomatology are negatively correlated with outcome. Length of time in treatment has been consistently shown to be positively related to outcome. No significant difference has been found in outcome between addicts who enter treatment voluntarily or under court order.

Counseling: Drug counseling is ubiquitously provided in most treatment programs. For clients with moderate to severe psychopathology, however, research has shown that providing psychotherapy in addition to counseling is more efficacious than providing counseling alone. Clients with low levels of psychopathology do as well with drug counseling as with counseling and psychotherapy.

Pharmacologic Treatments: Methadone is an orally-administered synthetic opiate that can be used in a medical maintenance program to treat the physiological aspects of opiate addiction. Research has shown that methadone maintenance is a successful treatment for opiate addiction, with retention rates that are better and outcomes that are equal to, or better than other treatment modalities. Even though addicts are frequently maintained on methadone for several years during resocialization, there is no evidence that long-term methadone maintenance has adverse medical consequences. Another therapeutic drug, naltrexone is a synthetic narcotic antagonist that blocks opiate receptors, thus preventing addicts from experiencing the euphoria associated with opiate use. Although patient acceptability of naltrexone generally is low, recent studies suggest that naltrexone may be appropriate with moderately impaired clients who are highly motivated to eliminate illicit opiate abuse.

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In the Anti-Drug Abuse Act of 1988, Congress provided funds to stimulate the development of new medications for the treatment of drug abuse. In response NIDA formed a medications development task force to oversee medications research. NIDA is proceeding with the development of pharmaceuticals that: reduce the craving for abused drugs, block the effects of abused drugs, moderate and/or eliminate the withdrawal effects of abused drugs, substitute for abused drugs with less toxic effects, block and/or reverse the toxic effects of abused drugs, and prevent (in special circumstances) the initiation of drug addiction.

Services Research: Critical areas of research currently include: the efficiency and effectiveness of alternative drug abuse treatment modalities, provider settings, and structures; cost benefit, cost offset, and cost effectiveness of different treatments; financing options; monitoring of trends in the provision, cost, utilization, and impact of drug abuse services; and the organization, delivery, impact, and quality of drug abuse treatment. Central to this research is the development of a body of knowledge regarding accessibility, acceptability, and receptivity to treatment. Important questions remain about what constellations of services are most appropriate for specific client types and for treatment of specific drugs of abuse.

Drug Abuse and AIDS

Intravenous drug abuse is a primary risk factor for HIV infection. HIV infection is primarily spread among intravenous drug abusers by needle sharing, a common practice that serves both practical and social functions. HIV infection is also spread sexually between intravenous drug abusers and their sex partners, and perinatally from intravenous drug abusers to their children. In 1988, approximately one-third of all reported AIDS cases were associated with intravenous drug abuse, with minorities being overrepresented among such cases.

Research has found that HIV seropositivity rates among intravenous drug abusers range from 0 to 65 percent in different cities, with the highest rates in New York, New Jersey, and Puerto Rico. HIV infection in intravenous drug abusers is increasing in many parts of the U.S., with lower rates among addicts in treatment than among addicts not in treatment. Research is also suggesting that HIV infection may be associated with "crack" and other forms of non-intravenous drug abuse due to users engaging in unprotected sex in exchange for drugs or money to purchase drugs.

Strategies for providing intravenous drug abusers with information about AIDS are currently being evaluated in large-scale demonstration research programs. These programs also collect data on demographics, drug use, needle sharing/cleaning practices, and sexual practices. They also serve as sources of information for intravenous drug abusers not in treatment.

Preliminary results from all reporting cities indicate improvements in needle hygiene practices and condom use for the study period.

ADDICTION AND NEUROBIOLOGY

Drug addiction is a disease of the brain. A thorough understanding of the relationship between the brain mechanisms which underlie behavior and how these processes are changed by drugs is essential to understanding drug abuse. It is also important for developing rational treatments for drug abuse and any resultant disease. The following discussion is concerned with the current concept of what constitutes drug addiction, the neurobiological basis for the rewarding aspect of drug taking, implications for developing treatment approachs, and a possible explanation for the difficulty in combating drug-abuse.

Biology of Addiction

Substrate For Addiction: The discovery of endogenous opioid peptides and their receptors in the brain has explained why opium from the poppy plant can bind to human brain and induce stupor. Endogenous opioids within the brain and spinal cord carry out specific functions. These substances are involved in the tempering of pain by drugs, in physiological events such as trauma and acupuncture, and in the physical dependence induced by opiates. Opiate narcotics, as well as barbiturates and alcohol, induce tolerance and physical dependence, the hallmarks of "addiction." In the dependent individual, the nervous system has adapted to the continued use of drugs so that it functions properly only when the drug is present. At this point, the individual needs the drug just to fell "normal," and drug seeking becomes motivated by the desire to avoid the painful consequences of drug abstinence. The changes in receptor functioning that occur during drug dependence and withdrawal are now being studied in order to develop interventions that might `reset' the nervous system to a closer to normal condition, thereby terminating dependence without severe withdrawal.

Brain Reward Circuitry - Basis For Drug Abuse: Although there has never been complete agreement on what constitutes drug addiction, classically this definition has included the development of tolerance and the induction of a profound physical withdrawal syndrome. Examples of classic addictive drugs are opiates, barbiturates, and alcohol. One drug that certainly does not fit this older definition is cocaine. Yet, the abuse of cocaine has reached epidemic proportions and treatment centers are filled to capacity with cocaine addicts.

In their efforts to explain the addictive properties of cocaine, neuropsychopharmacologists have proven, in animal and clinical studies, the hypothesis that certain drugs are sought because they directly activate the brain's reward system, a neural

network responsible for the subjective experience of pleasure. Events, activities, or stimuli are rewarding because this pathway is physiologically activated.

Efforts to map regions of the brain that animals would willingly work to stimulate have identified two specific dopaminergic projections of the ventral tegmental area (VTA) as critical links in the reward system. Dopaminergic projections are connections between the 'highest' brain center and other parts of the nervous system that are reactive to dopamine (a neurotransmitter). To produce reward, these projections must activate other dopamine receptors. Neuroscientists also found that animals will self-administer drugs directly into the reward circuit. Many types of abused drugs--including morphine, heroin, cocaine, amphetamine, and possibly nicotine--activate this system, albeit at different locations. This strongly suggests that drugs of abuse directly activate the brain's "pleasure centers", an effect that should, according to learning theory, lead directly to the repeated self-administration of these drugs by animals and people. This is exactly what happens.

Neurons containing opiate peptides and opiate receptors both play a role in this process. Hence, the reward circuitry involves both a dopaminergic and an opioidergic response. Other chemically coded responses are probably involved as well. This has led to an interesting question: is there a single brain reward circuit or several?

Separate Substrates for Reward and Dependence: Research has shown that, after initial exposure, drugs are sought by users simply because they induce pleasure. Not until later in the addictive process does physical dependence become a motivating factor in seeking drugs. This finding supports the quite remarkable notion that physical dependence and brain reward can be dissociated. The neurochemical proof for this separation of function came from experiments involving two specific regions of the brain, the VTA and the PAG. The VTA (the ventral tegmental area), which contains one of three principal dopamine producing areas) and the PAG (the periaqueductal gray region), a prominent anatomical relay station important in narcotic-induced temperance of pain transmission that is populated with opiate receptors. Experiments demonstrated that the PAG is responsible for physical dependence, while the VTA mediates the inclination to self-administer drugs.

Cocaine: A Potent Reinforcer: The strength of the rewarding ability of cocaine is illustrated by several animal drug self-administration studies. Cocaine was found to be inherently reinforcing; that is, no "priming" is necessary to induce animals to self-administer the drug. Priming is the exposure of an animal to a different drug to make him more reactive to the test drug. Morphine, on the other hand, usually requires physical dependence before self-administration will occur. Animals do not initially self-administer barbiturates, either. In fact, cocaine

is often used as the priming drug when training animals to self-administer. Cocaine is not unique in this respect, however. Heroin is also inherently reinforcing.

Another way to describe the rewarding value of a drug is with "breaking point" studies, an experimental approach which asks how many times an animal will press a lever to be rewarded with a single infusion of test drug. Animals have been reported to press a lever over 12,000 times for a single small dose of cocaine. This kind of abuse liability testing has made possible the characterization (and comparison) of drugs in terms of relative potency and/or reinforcing efficacy. Relative potency is that amount of drug the animal will work for relative to another drug. Reinforcing efficacy is the maximum number of lever presses for any dose of the test drug. Studies to date indicate that the reinforcing efficacy of cocaine far exceeds that of other stimulants. In fact, cocaine is so reinforcing that, when given unlimited access, animals will self-administer cocaine to their death.

Implications Of The Brain Reward Model Of Addiction: The brain reward model explains the "why" of drug abuse and brings the concept of "psychological dependence" into the realm of neurobiological events. The model may also provide the rationale for developing effective pharmacotherapeutic treatment strategies. According to the model, drugs are sought because they pharmacologically activate the brain reward system. The VTA is critical in the circuitry, and a variety of drug classes activate components of this neural system. Animal models used to test and elaborate the model have shown that brain dopaminergic neurons are critical in controlling drug self-administration, suggesting that dopamine antagonists should prevent drug self-administration. Surprisingly, however, greater clinical success with human cocaine abusers has been obtained with dopamine agonists, such as bromocriptine. The opposition between animal and human treatments may be due to the fact that, for animals, the physiological reward process is the principal determinant of the drug seeking behavior. Humans, by contrast, may have to contend with drug reward, drug craving, or both.

The effectiveness of bromocriptine prompted speculations concerning cocaine-induced dopamine depletions. Although there is little, if any, evidence for an actual dopamine depletion following cocaine use, there may be a functional shortage of neurotransmitter. A functional shortage is detected by a lack of response to the neurotransmitter. This may explain the purported treatment success with dopamine agonists. From a preclinical point of view, whether the most effective way to terminate cocaine abuse is to block cocaine-induced reward (dopamine antagonists to block reward/craving) or drug-induced neuronal changes (dopamine agonists to correct functional dopamine shortage) is not yet clear. Both possibilities are being explored.

Pharmacotherapy: The role of dopamine receptor subtypes in the investigation of the pharmacotherapy of cocaine is being examined. There are two types of dopamine receptors, termed D-1 and D-2, which are distinguishable by their localization in brain areas, their binding abilities, and the behavior they elict. One of the roles of the D-1 receptor is to enable D-2 functioning, i.e., the expression of behavioral events following D-2 stimulation requires D-1 receptor stimulation first. Several investigators have shown that D-1 antagonists can block the behavioral effects of amphetamine and cocaine.

Finally, inquiry has recently been made concerning a methadone-like pharmacological treatment for cocaine. Methadone, a weak opiate agonist, is used to treat opiate addiction--as long as it is taken, physiological processes are normal; craving for heroin disappears. Although cocaine does not induce physical dependence as opiates do, abstinence leads to an intense craving for more drug. Therfore, any drug that partially substitutes for cocaine would not only satisfy cocaine cravings, but would simultaneously activate the brain reward mechanism and thus stimulate cocaine-seeking behavior. People or animals detoxified from cocaine will relapse into cocaine use if they are exposed to the rewarding effects of another stimulant drug, like methylphenidate. There are clearly problems in trying to develop a replacement therapy for cocaine, though study of this approach has only begun.

Accomplishments

Drugs of Abuse and the Medial Forebrain Bundle: Abuse liability studies examine the reward properties of drugs of abuse by using a variety of measures of drug reward: self-administration, conditioned place preference (CPP), taste aversion, etc. In these studies, some drugs--for example, marijuana, quaaludes, and benzodiazepines--give false negatives; that is, they are not self-administered by animals, but they are abused by man. From such studies, two primary results have emerged over the past year.

For the first time, an animal paradigm for testing the abuse liability of marijuana was developed. In rats, a positive CPP was established for THC, the active cannabinoid in marijuana. It was found to be easier to establish a CPP in animals that had previously received doses of THC. (Interestingly, there are anecdotal reports which indicate that, in humans, the "marijuana high" has to be learned).

Separate abuse liability studies determined that two distinct receptors mediate different opiate effects. One receptor mediates positive affective potential, while another mediates analgesia. Evidence for this comes from the finding that naloxone, used in considerably higher doses than that required to prevent morphine-induced analgesia, could block a CPP established for morphine.

Drug Modulation of Cocaine-Induced Charges in Brain Stimulation Reward: In examining the time course of cocaine's effect on the threshold for brain stimulation reward (BSR) in rats, cocaine was found to produce a biphasic shift in affect. Cocaine caused an expected lowering of the self-stimulation threshold early in testing, followed 6-7 hours post-injection by a significant increase in the intracranial self-stimulation (ICSS) threshold. This later phase took about 9 days of testing to emerge. Two distinct phases are now apparent. One phase is characterized by reward system enhancement (euphoria) and the other by reward system depression (dysphoria). This later phase is much less well studied, but may actually be analogous to the clinical state of cocaine-induced dysphoria. This model holds much promise of a way to study these mechanisms.

Neural Substrate of Cocaine Reward: Since bromocriptine has been reported to be clinically effective in humans for reducing cocaine craving, the effects on the cocaine intake of rats were examined. Rats conditioned to seek cocaine and food were pretreated with bromocriptine. While this treatment caused a reduction in responses for cocaine, it did not for food. This selectivity of action, therefore suggests that bromocriptine may prove beneficial in the treatment of cocaine dependence.

Peptide Modulation of Mesolimbic Dopamine: It has long been speculated that Pavlovian conditioning plays an important role in drug abuse relapse; yet little information exists on the neural basis of the conditioned responses. To study conditioned reinforcement (CR), rats were trained to associate the presentation of food with a compound stimulus (light + click). After training, two levers were presented in the box for the first time. Responding on one lever resulted in the presentation of the conditioned stimuli only (no food). A response on the second lever had no consequences.

GBR12909, a cocaine-like drug (dopamine uptake blocker), produced, in a dose-dependent manner, a strong enhancement of the existing conditioned reinforcement. In a similar study, it was found that amphetamine also facilitated conditioned reinforcement when infused into the nucleus accumbens, but not when infused into the posterior striatum or anterior ventrolateral striatum. The results of these experiments suggest that enhanced conditioned reinforcement to psychostimulant drugs is mediated by dopaminergic stimulation of anterior medial sites within the striatum (including the nucleus accumbens). Studies of this type may provide the means to examine the biological basis of craving and/or relapse, and lead to an important extension of the brain reward model of drug abuse.

Dopamine Involvement in Opiate and Stimulant Drug Reinforcement: Work over the past year with an animal model of drug relapse suggests that the relapse process utilizes the dopamine reward mechanism. Once each day rats were trained to run a straight

alley to a goal box containing food. Upon completion of training, an extinction procedure was initiated in which the goal box contained no food. After running behavior had subsided substantially, a single reinforced trial was given, with the effects determined the next day. It was found that: (1) a simple reinforced trial during extinction was sufficient to reinstate running when animals were tested 24 hours later, (2) pre-treatment with haloperidol, a dopamine blocker, prior to a single reinforced trial, prevented the reinstatement of running 24 hours later. The latter finding indicates that the dopamine system plays a role in natural rewards.

Subsequently, this basic design was used to study amphetamine. It was found that rats would traverse a runway for a single 1.0 mg/kg s.c. injection of amphetamine. During extinction (saline injection instead of amphetamine), animals slowed their running behavior, but when given a priming injection, their running speed increased dramatically 24 hours later. If animals were pretreated with haloperidol prior to the amphetamine priming injection, their response 24 hours later was identical to that seen during extinction. This animal model appears to be comparable to human conditions where relapse is likely. Furthermore, this model expands the existing brain reward model and suggests a possible approach for studying relapse.

BEHAVIORAL PHARMACOLOGY

Behavioral pharmacology evolved from laboratory techniques used in the experimental analysis of behavior, developing as a separate discipline as these laboratory techniques were applied to pharmacology. The field of behavioral pharmacology is primarily interested in: 1) the use of behavioral methods to "screen" new chemical compounds for their liability to engender drug abuse or for their potential to treat psychiatric disorders; 2) the experimental analysis of the effects of drugs on behavior; 3) the determination of performance disruptions and incapacities due to acute or chronic administration of drugs, i.e., the "behavioral toxicity" of drugs; and 4) the use of drugs to examine generalizations, explanations, or hypotheses concerning behavior.

Behavioral pharmacology methods permit rigorous control of behavior with the establishment of stable behavioral baselines which can be used to evaluate the effects of specific drugs. These methods often permit the study of similar behavior in both animals and humans. Behavioral baselines can be used to determine the onset of drug action, the duration of action, and the residual effects of drugs. Drug effects can be evaluated not only on the performance of a learned behavior but also on the learning of new behaviors. In addition, one may also determine the effects of other experimental manipulations on drug-behavior interactions, such as the antagonism of cocaine effects on behavior. The discipline of behavioral pharmacology is useful in

studying therapeutic efficacy, possible side effects, and the abuse potential of new chemicals, as well as established medications.

Current Status Of Behavioral Research On Drug Abuse: Behavioral research on drug abuse today is encompassed by three main topics: 1) a new conceptualization of what constitutes an abused drug, 2) a capability to evaluate drugs for abuse liability, and 3) the ability to study clinically-relevant behavioral aspects of drug abuse in humans.

Conceptualization: abused drugs as reinforcers of behavior: In large part due to the animal model of self-administration, behavioral pharmacology has been instrumental in developing one of the more generalizable concepts of the drug abuse field, namely, that an abused drug is a reinforcer. This simple but powerful concept means that an abused drug has the combined properties of both positive reinforcement (often termed "euphoria" or a "high" in humans) and negative reinforcement ("relief" in human terms from dysphoria, withdrawal symptoms, anger, loneliness, etc.). The implication of this concept is that the scientific information on positive and negative reinforcement, previously gathered by behavioral psychologists over several decades, can be brought to bear on the many problems of drug abuse.

Thus, the long chain of behaviors involved in preparing for, seeking out, and finally self-administering a drug can be properly viewed as being maintained by the drug's reinforcing properties. Considering the many factors (psychological, physiological, societal, genetic, and others) associated with the etiology of drug abuse, the concept that the chemical itself has inherent reinforcing (and therefore addictive) properties is an important contribution to our understanding of the causes of drug abuse.

Testing abuse liability: The research basis for testing abuse liability originated with the self-administration technique developed for primates (described above). This technique, as refined and modified for many classes of compounds (including opioids, barbiturates, benzodiazepines, and stimulants), is capable of giving a highly reliable evaluation of the addictive liability of almost any new compound. For instance, before new psychotropic medications (particularly analgesics) are proposed to the Food and Drug Administration for medical use, they are frequently tested using this laboratory model of self-administration. Currently, the model has been successfully generalized to human subjects. Now, questions uniquely appropriate for the human species can be answered.

The second technique, the drug discrimination model, is also used to identify potential drugs of abuse. The basis for this technique is the subjective effect of abused drugs often referred to as euphoria. Thus, an animal can be trained to discriminate

internal stimuli (just as it can be trained to discriminate external stimuli such as a tone or a red light) and to make a particular response on the basis of this discrimination. For example, a trained rat will press the left lever when injected with heroin and the right lever when injected with placebo. Then, when a drug with similar internal stimulus effects is injected, the animal will press the left lever. Codeine, morphine, meperidine, etc. cause the same reaction. The drug discrimination model is technically much easier to establish in the laboratory, particularly with groups of animals, than the self-administration model.

Clinically-relevant behavioral aspects of drug abuse in humans: Much of the early development in the behavioral pharmacology of abused drugs occurred in the animal laboratory. The criticism at that time, was that the results were questionable because animals and humans were different. Today, however, in large part because of the extensive development of behavioral pharmacology research in humans, this criticism is no longer valid. Some of this research involves self-administration; some involves drug discrimination; some involves studies of complex performance. These methods have evolved from the animal laboratory, although the human techniques are now far more sophisticated. In addition, there has been an upsurge in research methods to study a wide variety of issues relevant to drug abuse. Some of these studies are: drug "craving" and the reduction of craving by other variables including medications; simulations of the disruption by abused drugs on driving an automobile or piloting a plane; performance on psychological tests of intellectual functioning. The science of the behavioral pharmacology of drug abuse has developed usefully and has a broadened focus which includes a wide variety of topics relevant to substance abuse.

Accomplishments

Effects of Prenatal Exposure to Abused Drugs on Infant Behavior: Current research is designed to enhance the understanding of the developmental consequences of prenatal drug exposure and the effects of being reared in a substance-abusing family. Eighteen children, 15-18 months old, were prenatally exposed to phencyclidine (PCP). They were compared to a sample of high-risk pre-term children who were of similar socioeconomic status, ethnicity and from single parent households. The drug-exposed children were found to have significantly lower developmental scores but still were within the low average range. Because in standardized assessments the examiner directs the tasks for the child, children may appear more competent than clinicians judge them to be. Therefore, the research protocols included an unstructured free play situation that required self-organization, self-initiation, and follow-through without the assistance of the examiner.

In this context drug-exposed children show striking deficits. They have significantly less representational play than high-risk

pre-term children. Play for the majority of the drug-exposed children was characterized by scattering, batting, and picking up and putting down the toys rather than sustained combining of toys, fantasy play, or curious exploration. Almost all of these infants have some ataxia, intentional tremors, and a static stare that resembles a type of autism. When the PCP-abusing mothers were subjectively evaluated, they appeared immature, less sensitive, and less accepting of their children than the control mothers.

The impact of these findings is potentially enormous. Children of substance-abusing parents live in unstable, often dangerous environments, cared for inconsistently by parents impaired by chronic drug abuse. Postnatal environmental factors and the possibility of prenatal biological impairments pose grave risks to the childrens' health, to the extent that normal development must be considered threatened.

The use of cocaine by pregnant women has had a tremendous impact on maternal/child health care in this country. Through funding from the National Institute on Drug Abuse, the program at Northwestern University Medical School has examined the effects of cocaine use on pregnancy outcome and the neonate. In the past year, published articles have documented: 1) an increased rate of genitourinary tract malformations in cocaine-exposed infants, 2) toxicological effects of cocaine passed via maternal breast milk, and 3) the effects of temporal patterns of maternal cocaine use on pregnancy outcome and the neonate.

The most recent study shows that women who use cocaine in only the first trimester of pregnancy have improved obstetric outcome with a decreased rate of premature delivery, abruptio placentae, and intrauterine growth retardation when compared to women who use cocaine throughout all three trimesters of pregnancy. However, even if a woman ceases cocaine use in the first trimester of pregnancy, the neurobehavioral outcome of the newborn infant is still impaired.

Since cessation of cocaine use in the first trimester improves pregnancy outcome, this information supports early intervention programs for pregnant women. These studies also highlight the need for prevention programs across the country. This is particularly so since cocaine use, even if terminated in the first trimester, still results in neurological changes in the newborn. Long-term evaluation of the growth and development of prenatally cocaine exposed infants is underway.

Inhibition of Cocaine Self-Administration: Results from an animal model suggest that buprenorphine may have direct antagonist actions upon cocaine self-administration. Buprenorphine is an opioid that has mixed neurochemical actions in the body. It has actions similar to opiates while at the same time antagonizing opiates. It potentially may be useful for the treatment of opiate addiction since it appears to produce little

physical dependence in humans.

In the animal model, monkeys were initially trained through operant behavioral procedures, to press a lever to receive a banana pellet and at another time, to self-administer intravenous cocaine. Daily treatment with buprenorphine resulted in an 80 percent decrease in cocaine self-administration at the end of 5-days. Buprenorphine initially reduced food administration by only 25-30 percent, and later not at all. This indicates the selective inhibitory effects of buprenorphine on cocaine self-administration. Future studies are planned describing the degree of the blockade provided by buprenorphine. The possibility that buprenorphine might be effective as a treatment for cocaine abuse has been received with considerable interest by the drug treatment community.

In terms of safety, buprenorphine did not interfere with the ability of pigeons to complete a complex behavioral task. Methadone, however, did disrupt the pigeons' learning ability. These findings suggest that buprenorphine may have fewer deleterious behavioral side effects than methadone.

Buprenorphine is not the only pharmacologic agent being studied, however. A number of pharmacotherapeutic agents have been tested in a rat model of intravenous cocaine self-administration. Treatments with Fluoxetine, an antidepressant, reliably reduced cocaine self-administration by at least 50 percent. Self-administration of cocaine rapidly returned when the 5-day treatments were finished. A study in progress is also showing that Tegretol, (carbamazepine) an antidepressant that is actually used as an anti-seizure drug, is also effective in reducing cocaine self-injection in rats. Controlled studies show that Tegretol, but not Fluoxetine, decreases behavior maintained by a non-drug reinforcer. Thus, the mechanism of action of Fluoxetine may be to selectively interfere with the reinforcing effects of cocaine.

Past History as a Determinant of Present Drug Use: In research in which rats were trained to drink ethanol from two bottles in the testing cage, glucose solutions were temporarily substituted for ethanol in one of the drinking bottles. For one group of rats, the glucose solution was concentrated and highly acceptable; for the second group the glucose solution was dilute and much less acceptable. Then, after a prolonged period during which only ethanol was available in the drinking bottles, the animals were tested for ethanol/glucose preference. The group that had previously received the highly acceptable glucose solution was found to drink much less ethanol across a wide range of glucose concentrations. These results offer convincing experimental evidence for a common belief that the tendency to abuse drugs is related to early experiences with drug use. The results also show that rewarding alternatives will reduce drug use. Research on the role of past history as a determinant of present drug use is continuing.

In another study rats were exposed either to water, a cocaine solution, or an ethanol solution. Under the appropriate experimental conditions the animals drank copious quantities of each of the solutions. When fluid intakes stabilized, the drinking fluid was changed to the benzodiazepine drug, Librium. Intake of Librium was greater for the ethanol history rats than for the water history or cocaine history groups. This observation is consistent with human studies which indicate that a history of ethanol or sedative abuse increases the probability that benzodiazepines will be abused.

Abuse Potential of Inhalants: The abuse of inhaled solvents is one of the least studied substance abuse phenomena. Studies have been conducted on the behavioral effects of various inhaled solvents using variations on animal models to evaluate the abusive properties of drugs and alcohol. One major finding from this research is that certain widely-abused inhalants, such as toluene and methyl chloroform, produce behavioral effects very similar to those of abused depressant drugs such as alcohol and the barbiturates. This finding has led to the hypothesis that solvent abusers are seeking to achieve an alcohol-like intoxication. With animals trained to discriminate alcohol administration from placebo administration, a number of solvent vapors produce effects similar to those of alcohol. In addition to toluene and methylchloroform, this is also a property of low concentrations of certain anesthetic vapors such as halothane. This animal model may be used to classify solvents that produce these effects and may be able to predict the abuse potential of selected vapors.

Tobacco Dependence: Nicotine polacrilex gum (Nicorette 2 mg), when used in adequate amounts, can prevent the weight gain that is so common following smoking cessation. These findings are encouraging for smokers who want to quit but do not want the associated weight gain. Smokers should know, however, that weight gain may occur anyway once use of nicotine gum is stopped. Therefore, additional strategies may be needed if weight gain is to be avoided entirely.

Withdrawal symptoms, including irritability, anxiety, and impatience, are apparent for about 5 weeks after smoking cessation. During this time, symptom intensity declines steadily in smokers who do not use nicotine gum. Some symptoms, however, particularly increased hunger and eating, remain elevated for at least 10 weeks after smoking cessation. Nicotine replacement therapy effectively suppresses most of the symptoms associated with tobacco withdrawal. Smokers who quit without the aid of nicotine replacement therapy must be prepared for a longer period of withdrawal discomfort.

Relapse due to undesirable weight gain is common. One study has provided the first demonstration in humans that nicotine alone produces increased metabolic rate at rest. A study examining the

metabolic effects of nicotine in conjunction with light physical activity demonstrated that the metabolic effects of nicotine were more than twice as great during activity than during rest. Another study examined the effects of brief (one week) smoking cessation on caloric intake, activity, and metabolic rate in females. The general findings were substantial increases in caloric intake and a slight decline in resting metabolic rate with no change in physical activity during the week of smoking cessation. These changes reversed with resumption of smoking. Results of these studies may help determine specific effects of smoking and nicotine on energy balance. Furthermore, they suggest which adjunct procedures may be most promising in limiting weight gain, and thus smoking relapse.

BIOMEDICAL ASPECTS OF DRUG ABUSE

Basic research in drug abuse during the past 20 years has led to findings that not only have revolutionized our thinking about the biological mechanisms that underlie the addictive process, but which also have led to a clinical applications in other areas of medicine.

Medical Implications

Opiate Receptor/Peptides: The discovery of opiate receptors and endogenous opioid peptides in the mid 1970s by NIDA-funded scientists led to more than a decade of extensive research on opiate receptors that culminated in the description of a number of subtypes of receptors, each with a different anatomical distribution and possibly different functions. Also, about a dozen endogenous opioid peptides have been identified.

The concept of drug agonists and antagonists is extensively used to describe the effects of potential treatment drugs. Agonists are drugs that produce very similiar effects as the 'primary' drug; antagonists block the effect of the primary drug. One important finding is that the so-called mixed agonist/antagonist types of opiates can produce marked analgesia with less addictive potential than pure drugs, such as morphine. Some of these drugs are on the market, including pentazocine, nalbuphine, and butorphanol.

Experimental work with pure antagonists (such as naloxone and naltrexone) has also yielded findings that may have diverse clinical applications, e.g.in haemorrhagic, septic or spinal shock, suppression of appetitive behavior, stimulation of peristalsis in pathological constipation, various effects on memory, reduction of psychiatric symptoms in some psychotic patients, and in treating some infants at risk for Sudden Infant Death Syndrome (SIDS). Preliminary results hold promise of important therapeutic applications, even though the physiological mechanisms remain obscure.

There are three families of opioid peptides: beta-endorphin, enkephalin, and dynorphin. Each family has a different binding strength to each subtype of opiate receptor. Also, at least three major types of opiate receptors have been defined. The mu receptor binds morphine, the delta receptor binds enkephalins, and the kappa receptor binds the prodynorphin products.

Products from a single peptide family can interact with more than one opioid receptor, and a single receptor can receive signals from more than one peptide family. There is no rigid association between opioid peptides and particular receptor types. Therefore, the activation of an opioid circuit is determined by which opioid peptides are physically adjacent to it, rather than by some theoretical rank order of preference.

Phencyclidine: PCP was synthesized for clinical use as an analgesic during the 1950s, but withdrawn from licit human use several years later. It has been used illicitly as a psychedelic since the 1960s. Since its introduction into the illicit drug market, PCP has had an uneven incidence of abuse; peaking in the late 1960s as an oral drug and, again, in the late 1970s, after smoking PCP-laced cigarettes became popular. The movement of PCP abuse from suburban and college student populations to inner cities has resulted in fewer people abusing the drug, but in higher use per addict. This has resulted in an increase in the number of severe toxic reactions.

Studies on the pharmacology of PCP in both man and animals has shown that a complex set of symptoms including both stimulant and depressant effects are produced by the drug. Both people and animals can discriminate PCP from LSD, cocaine, narcotics and neuroleptics. In addition, animals will self administer PCP, maintaining nearly continuous intoxication if the drug is freely accessible.

Dual Receptors: A neurochemical breakthrough that helped to conceptualize the relationship of behavior to neurobiology occurred in 1983 when investigators offered convincing evidence that PCP acts at two different receptors (the PCP and the sigma site) in the central nervous system.

PCP binds strongly to the PCP site but slightly less to the sigma site. Not only do these two sites have different binding characteristics, but they are distributed quite differently in the nervous system. PCP has abundant binding sites in areas of the brain associated with perception and emotion. By contrast, the sigma site is concentrated most densely in areas of the brain associated with thought and connecting areas.

Drugs that bind to PCP receptors are all agonists that produce feelings of well being and have anti-anxiety effects at low doses. At higher doses PCP affects motor coordination by causing postures to "freeze" (catatonia); movements to be constantly

repeated (stereotypy); and irregular coordination (ataxia). Chronic use of PCP results in loss of long term memory.

Both agonists and antagonists bind sigma receptors. The agonists induce increased movement from place to place and psychiatric-like symptoms. Sigma antagonists reverse agonist effects, such as psychiatric-like responses. Sigma agonists have very low binding strengths for dopamine receptors yet seem to act indirectly at dopamine terminals to produce increased activity and disordered muscle tone.

PCP inhibits the activation of a specific kind of receptor called N-methyl D-aspartate (NMDA) receptor. This receptor is activated by the neurotransmitter, glutamate, the most abundant, excitatory neurotransmitter in the brain. This inhibitory activity is clinically important because PCP can be of great value for treating strokes to prevent or reverse the neurotoxic effects of excess glutamate release that occurs during hypoxia (low oxygen) or ischemia (low blood supply). Synthetic drugs chemically related to PCP can be designed to bind NMDA receptors, thereby reducing neurotoxic damage.

Changing Concepts of Tolerance and Dependence: Pharmacological research has played a major role in the formulation of concepts regarding tolerance and dependence to abused drugs. Opiates are the prototypic drugs of abuse for which tolerance and dependence were first recognized and shown to contribute to the addictive process. It is now clear, however, that tolerance and dependence can also develop to many other drugs, including stimulants, hypnotics, depressants and hallucinogens. As knowledge about these phenomena has increased, certain ideas have been reevaluated and modified.

Tolerance: Recently, a combined pharmacological and neurophysiological approach has shed new light on the molecular mechanisms of tolerance. These studies suggest that the opiate receptor linkage to the second messenger system (which relays the message within the cell) is altered in the tolerant state. Apparently, after tolerance has developed, the receptor is no longer as effective in activating the second messenger.

Despite the lack of a clear understanding of the mechanisms responsible for the phenomenon we call tolerance, we can define the term operationally, either as the reduced effect of the same dose of a drug with subsequent administrations, or as a need to increase the dosage in order to maintain the same level of effect. This simple definition covers the roles of a variety of pharmacokinetic, pharmacodynamic, and other mechanisms involved in the tolerant state.

Dependence: Traditionally, dependence also has been defined in operational terms. It is described by the physiological and psychological symptoms that appear when the drug is withdrawn or antagonized ("abstinence syndrome"). The abstinence syndrome can

after a dose, a state of "pseudoequilibrium" is reached between plasma and tissues; THC is then eliminated from the body at a much slower rate. This slow elimination process is primarily due to the slow return of THC from fatty tissues to blood. Using sensitive analytical techniques, THC metabolites can be found in plasma for up to two weeks and in urine for up to 31 days. Laboratory investigations have reported that THC may affect complex performance skills for up to 24 hours after drug ingestion.

The smoking of cocaine is reported to induce a rapid, temporary, euphoric state of great intensity. Pharmacokinetic studies of cocaine indicate that the peak plasma cocaine level is rapidly reached within five minutes of smoking. The plasma cocaine profiles are almost equivalent to those following an intravenous dose. This rapid delivery of cocaine to the brain by smoking explains the increased use of cocaine by this route. Cocaine is rapidly metabolized and eliminated from the body primarily as metabolites in urine. The half-life of cocaine in blood is about 1-2 hours.

Pharmacokinetic and pharmacodynamic studies of cocaine demonstrated that tolerance develops rapidly to cardiovascular and euphoric effects of cocaine, with the intensities of both increasing to peak levels and then declining despite the presence of a constant cocaine plasma concentration. Tolerance to the euphoric effect of cocaine is virtually complete and the sensation of "high" is often replaced by a dysphoria. This finding confirms anecdotal information that the cocaine user on a "run" of repeated doses finds that continued use eventually fails to produce the desired effect.

Accomplishments

Cocaine and Cardiovascular Toxicity: Research has shown that cocaine effects dose-dependent changes in blood pressure, heartrate, and the rate-pressure product (an index of heart tissue oxygen consumption). The dramatic increases in the rate-pressure product suggests an increased risk of heart attack in individuals with existing compromised coronary blood flow. Blockade of the sympathetic nervous system or decreasing the brain's activity inhibits the blood pressure response to cocaine. The effects of cocaine, therefore, on the cardiovascular system are dependent on integrated central nervous system responses, peripheral activity, and amount of cocaine.

Detection of Cocaine in Saliva: The potential of saliva and hair, to be used in lieu of urine, in screening for cocaine use, are currently under investigation. Preliminary data show cocaine levels in saliva are substantially higher than in plasma, suggesting that saliva may be a useful, practical marker of recent cocaine use. Studies also are examining the time course of cocaine its primary metabolite in hair after the clinical administration of cocaine. Preliminary data indicates that

be reversed by re-administering the drug or another one with similar effects. As our knowledge about dependence has grown, however, acceptance of such a simple definition has waned. Dependence is really comprised of two components: the abuse liability of a drug (potential for abuse) and its dependence potential (potential for behavioral and/or physical signs of abstinence).

Changing Concepts: In recent years many generally accepted ideas about tolerance and dependence have been revised. Some of the concepts that have emerged are the following: Although tolerance and dependence are usually linked, they are not always; even though chronic administration of a drug is usually required to produce tolerance and dependence, under certain conditions, even a single dose can result in these effects; tolerance does not develop equally to all effects of a drug and reverse tolerance (increased responsiveness or sensitization) can occur; drugs usually exert their effects on more than one receptor type or subtype; species differences and genetic determinants of responses to drugs of abuse, after both acute and chronic exposure, are being discovered.

Binding studies continue to examine the effect of repeated opiate administration on the binding strength and number of receptor types. One study has shown a difference between the effects of heroin and morphine on mu-opiate receptor activity, suggesting that tolerance development to all opiate drugs may not proceed in the same way. The central puzzle, however, in opiate tolerance development is a loss of receptor responsivness. In other words, even when opiates do bind to the receptors of tolerant animals, the consequences are not the same as those prior to the development of tolerance. Relatively less is understood about the cellular mechanisms of physical dependence. Nevertheless, the recent advancements in understanding tolerance-related phenomena are likely to pave the way to a better understanding of mechanisms of physical dependence.

Metabolism, Distribution and Pharmacokinetics: Information on pharmacokinetics and pharmacodynamics is important in understanding drug effects on the body and in designing effective treatment strategies for drug intoxication and drug addiction. Pharmacodynamics research involves the identification of metabolites, the elucidation of metabolic pathways, and the quantitative description of absorption, distribution, metabolism and excretion of a drug in the body. Pharmacokinetics is a quantitative description of the time course of effects.

Marijuana is one drug that has been well studied. It contains more than 420 chemical compounds including at least 61 cannabinoids, a class of chemicals unique to the cannabis plant. Among cannabinoids, delta-9-tetrahydrocannabinol (THC) is the major psychoactive component. Following a single intravenous dose, plasma THC levels decline very rapidly over the first few minutes and then at a much slower rate. Approximately six hours

cocaine can be found in hair, but minimum dose detectable is still under investigation.

PSYCHOSOCIAL EFFECTS

Over the past several decades, widespread abuse of licit and illicit drugs alike has produced serious socioeconomic, psychosocial and health consequences.

Psychosocial and Other Health Effects in Young Children and Adolescents : Drug abuse occurs in stages. In general the abuse of licit drugs (alcohol, tobacco, so called 'Gateway Drugs') begins early in life and progresses to illicit drugs like marijuana, cocaine, PCP, heroin, and others. For young adults, a key risk factor for initiation into advanced stages of drug use is peer influence and peer's use of marijuana. Furthermore, a national study has shown that youth who abuse drugs tend to drop out of school prematurely and that early drug abuse may lead to delinquent behavior. These adolescents tend to enter late into the conventional roles of adulthood, such as marriage and continuous employment. The data show that adult drug abuse can be predicted by the extent of adolescent illicit drug abuse, particularly among men. Finally, the use of drugs, dropping out of school, and deviant behaviors are associated with early sexual involvement and premarital pregnancies, both of which are undesirable because of concerns about AIDS, and babies born to addicted mothers.

With a few notable exceptions, initiation into drug abuse usually occurs by an individual's mid-20s. Initiation into cocaine use seems to increase after age 19, and, between the ages of 19-24, the rate of initiation into prescribed psychoactive drugs is almost double the rate of initiation into illicit drugs. While marijuana users generally tend to stop using it at about age 25, a study conducted in New York public schools, suggests that the persistence of illicit drug use is greatest in the adults who initiated drug use during adolescence.

Why do some drug users stop using? Those who use drugs in response to social influences are more likely to stop using than those who use for psychological reasons. Data support the hypothesis that the factors that predict cessation of drug use in adulthood (participation in conventional social roles, good health, and the prior degree of involvement with illicit drugs) are similiar to those that predict lack of initiation in adolescence. For marijuana, degree of prior drug use is the strongest predictor of continued use, while the strongest predictor for cocaine is the degree of use by friends.

Drug Abuse, Children, and Family Interactions: Drug abuse by family members such as parents and older siblings can significantly affect an adolescent's attitude towards drug abuse, and often correlates with early first-use. Children of drug

abusers are more likely to be neglected, abandoned, and even when remaining with the family, less likely to interact with parents. They are at higher risk of emotional maladjustment, and of developing deviant and aggressive behaviors, including crime. Furthermore, attitudes of drug abusing adolescents toward sexual activity, pregnancy and childbearing are promiscuous and less responsible.

The role of familial factors in alcoholism has been shown, and these factors may also contribute to development of drug abuse among adolescents. A study involving interviews with 467 middle- to high-income families found that fathers were more likely to report drug-related problems if their parents had had drug-related problems, and were even more likely to have such problems if their spouses did as well. Mothers were less likely to experience problems if their parents had had drug-related problems, but were significantly more likely to experience these problems if their husbands did. Parental divorce was a strong and significant predictor for alcohol/drug problems for male adolescents. Boys from broken homes are more likely to have drug related problems than boys from intact families. Divorce, however, is not a significant predictor for girls.

Maternal and Paternal Drug Abuse and Its Consequences: With drug abuse among pregnant women on the rise during the past few years, as many as 375,000 infants may be affected from in-utero exposure to drugs annually in the U.S. Obstetrical and neonatal complications have been reported historically in association with the use of alcohol, opiates, and other drugs during pregnancy. Recently, more serious problems are being reported in women who used cocaine and marijuana during pregnancy. In one study examining the consequences of maternal drug use, about 16 percent of the women denied using marijuana and 24 percent denied using cocaine, even though the urine toxicology was positive. This strongly suggests that self-reports may not be totally reliable predictors of drug use during pregnancy.

While the effects of cocaine use by pregnant women are better documented than use of marijuana, the preliminary results of a multiyear study suggest that long-term marijuana use by pregnant women impairs, in a dose-dependent fashion, their childrens' memory up to age four.

Women, however, make only a partial contribution to the health of their fetus and information regarding fetal and offspring consequences of drug abuse by fathers is virtually nonexistent. However, data from animal studies suggest that morphine administration in the male rat just prior to and during puberty produces significant effects on the development of their male progeny via reductions in male hormone levels. The effects persisted from early in life through adulthood suggesting that exposure to opiates early in life may have long term effects on the development of male offspring. Additional studies in humans will be necessary to confirm these findings from animal studies.

DRUG-CRIME CONNECTION

During the past year NIDA has actively funded research examining the drug-crime connection. Findings have been utilized by policy makers, drug enforcement officials, and health and human services providers to develop effective strategies in their war against illicit drug use and drug-related criminal activities.

Drugs and Crime: Two schools of thought on the drug-crime nexus emerged since the 19th century: the medical model and the criminal model. While the criminal model of drug abuse argued that addicts ought to be the objects of vigorous police activity, proponents of the medical model on drug abuse postulated that drug abuse was a chronic and relapsing disease, and any individual suffering from this disease should be dealt with as any other patient suffering from a psychological or medical disorder.

Not until the late 1960's and earlier 1970's were accurate data collected on the nature and extent of drug-related crimes, the criminal involvement of narcotic users, and the casual linkages between drug use and criminality. A pioneer in this study, Saul Sells, from Texas Christian University, was supported by NIDA to develop the Drug Abuse Reporting Program (DARP). DARP provided a national treatment data base of over 42,000 drug abuse patients, some of whom were admitted into treatment more than once. These data demonstrated so conclusively that the vast majority of patients were involved in criminal behavior prior to treatment that the concept of crime-free days was developed and used as one criterion of treatment outcome evaluation.

For example, results of a study that explored the criminal careers of 243 addicts over an 11-year period indicate that the typical addict was involved in more than 178 criminal offenses per year. If these results are generalized to the estimated 450,000 heroin addicts in the United States, it can be postulated that narcotic addicts commit over 80 million crimes per year.

In a similar study the criminal careers of a group of 573 active narcotic addicts were analyzed in detail. For the preceeding 12 months, this cohort reported committing 375 crimes each. Of the total offenses reported, 38 percent involved drug sales, and an additional 22 percent included other "victimless crime" such as prostitution, procuring, gambling, and alcohol violations. The remaining 40 percent included robbery with assaults, vehicle theft, shoplifting, selling stolen goods, forgery and counterfeiting, burglary, pickpocketing, larceny, fraud, and other crimes. Results suggest an arrest rate of just 0.2 percent.

Research in the early to mid 1980's focused on analyzing, in more detail, the addict's criminal career history and the economic

aspects of this relationship. The prevalence of illicit drug use among prisoners and the drug-violence relationship were also analyzed. This research has yielded interesting results.

Studies of the economic burden of active heroin addicts have shown that daily heroin users commit a disproportionate number of crimes, costing society around $55,000 per year per addict. The most common crime other than drug dealing was robbery.

Of all arrestees, 33 percent tested positive for cocaine metabolites, 66 percent were positive for marijuana and 11 percent for PCP. Urine samples also showed that 29 percent tested positive for two or more drugs. Moreover, those charged with a drug offense were more likely to have used cocaine than other drugs.

Criminal Careers of Narcotic Addicts: Recently released findings of a NIDA-funded study which has been following a group of 253 narcotic addicts in New York City and Baltimore indicates that the use of non-narcotic drugs (e.g. cocaine, PCP, marijuana, alcohol) is higher during periods of narcotic addiction than narcotic abstinence. Further, during periods of narcotic abstinence, the use of all drugs decreases. These findings imply that the recruitment of addicts into treatment for their non-narcotic drug abuse may be most favorable when non-narcotic drug abuse is at its lowest.

Preliminary results of another study that is collecting data on the criminal activities, drug use behavior, and psychological well-being of a group of narcotic addicts and their peers, who were first interviewed more than 10 years ago, indicate that a significant percentage of addicts' peers were also addicted to heroin and other drugs. There also appear to be significant within-race differences among peers and addicts. A much larger proportion of white addicts show significant psycholocial distress and report higher levels of anxiety, depression, and impaired cognitive functioning than do black addicts.

Serious Drug Use by Juvenile Delinquents: Results from a Miami, Florida, study suggest that crack use among juvenile delinquents is extremely high, and that crack use is linked to a higher rate of criminal activity among these delinquents. Overall, each youth interviewed could claim responsiblity for nearly 900 criminal offenses during the 12 months prior to interview. It appears, therefore, that crack users, like the heroin addicts of the 1960's and 1970's engage in a high number of criminal activities.

In the Miami study, the majority of those interviewed began their drug using careers at age 7 with alcohol experimentation; all had been "high" by age 8. The majority proceeded to regular use (3+ times per week) of alcohol by age 9. Marijuana use began by age 10, followed by regular use by age 11. Cocaine use occurred next, with 98 percent of the sample trying the drug before age

12--and becoming regular users less than a year later.

Experimentation with heroin, speed, and prescription depressants was clustered in the early part of these juveniles' 12th year. Half moved on to the regular use of depressants, 20 percent reported the regular use of heroin, less than 5 percent used speed regularly. Some 97 percent reported experimentation with crack -- before age 13; the overwhelming majority of these moved on to the regular use of crack within a few months. When those interviewed were asked what drugs they preferred, the overwhelming majority indicated a preference for crack, followed by marijuana.

Drug Use and "Crack" Business Involvement: Current drug use rates among the Miami delinquents varied considerably by degree of participation in the crack trade. Of the 254 youths questioned, 80 percent indicated various levels of involvement in the crack business. Eight percent were involved only peripherally since they sold the drug only to their friends, worked as lookouts for dealers, or steered customers to crack houses. Most of the youths were crack "dealers," involved directly in the retail sale of crack. Finally, 18 percent were designated as "dealer+," since they not only sold the drug, but also manufactured, smuggled, or wholesaled it.

The greater a youth's involvement in the crack business, the more likely he/she was to use drugs such as marijuana, depressants, and crack on a daily basis. The most pronounced differences are with crack use. The proportion using crack daily ranged from 2 percent of those with no crack business involvement, to 87 percent of those in the dealer+ group.

The Criminal Justice System and Drug Use: A recently completed NIDA-funded study in Maryland determined the influence of the criminal justice system in deterring individuals, who had been arrested and tried for marijuana possession, from continuing marijuana use. The researchers interviewed a representative sample of all individuals tried for possession of marijuana and a comparison group who were marijuana users but had not been tried for marijuana possession. Fifty-eight percent of those selected to be interviewed received a verdict of guilty, 23 percent received probation before judgment (PBJ), and 19 percent were found not guilty.

Subjects in both groups were interviewed twice. The first interview was scheduled for two months after adjudication and the second interview one year later. The verdict of probation before judgment (PBJ) under Maryland law is an alternative to the guilty verdict. Judges may assign the verdict of PBJ to individuals found guilty, but with no prior conviction for a controlled dangerous substance (CDS) charge. The judgment of guilty is withheld pending completion of the terms of probation. If the terms of probation are completed satisfactorily and no new criminal charges are filed during the probationary period, the

verdict of guilty is not entered into the official files, and the record of the proceeding is expunged. However, if the terms of probation are not met, or if there are subsequent CDS charges, the verdict of guilty is entered on the permanent record.

Results suggested that the trial experience had little effect on the subjects' drug use. Ninety-four percent of those using marijuana before arrest were using marijuana within two months post trial. Self-report information on marijuana use in the 2 months prior to the arrest period indicated that 91 percent of the tried population and 83 percent of the control group were using marijuana. Thus, it seems that marijuana use after trial is not impacted at all by formal judicial proceedings.

Despite the high rate of relapse, the verdict received did impact post trial marijuana use. Individuals who received a verdict of PBJ, were more likely to reduce their marijuana consumption than those who received a verdict of guilty or not guilty. Almost half of the group that received a verdict of PBJ reduced their marijuana use, while less than a third of the guilty verdict group only reduced their use. It seems possible that individuals who received PBJ saw this sentence as an incentive to reduce their marijuana use. Apparently the other groups were not similarly motivated.

DATA COLLECTION

In order to understand the nature and extent of the drug abuse phenomenon, NIDA conducts and supports research on the incidence, prevalence, morbidity, mortality, and other adverse health consequences associated with drug abuse. Many of NIDA's surveys are ongoing and provide trend data on drug abuse prevalence, incidence, and consequences. Incidence and prevalence estimates and related adverse effects are available for each major drug type. Research is not limited to estimating the magnitude of the problem, but also includes examination of variables which may define and explain behavior patterns and sociodemographic characteristics of drug abusers. With data collection systems in place to monitor changes and trends, it is possible to develop effective public health strategies for intervention and control.

NIDA Surveys

Recent surveys have assessed drug abuse prevalence in the household population of the United States for a number of

The National Household Survey on Drug Abuse has been sponsored by NIDA since 1974 and is conducted every 2 to 3 years with the latest conducted in 1988. This national prevalence survey is the single most important measure of trends of drug abuse in our population. Using standardized methods to maximize response validity, trained interviewers administered questionnaires to respondents in their homes. Self-administered answer sheets were

also used. All data are confidential and anonymous. Questions address use of substances including marijuana, cocaine, hallucinogens, psychotherapeutic drugs, alcohol and cigarettes. Respondents are randomly selected within age categories from a national sample. In order to obtain more stable estimates of drug use for specific groups, young adults (age 12-34), blacks and Hispanics have been oversampled since the 1985 survey.

The most recent Household Survey results were issued in July, 1989. The survey found significant reductions in overall drug use between 1985 and 1988. The number of current illicit drug users dropped from 23 million to 14.5 million. Current cocaine use dropped by 50 percent, but no reduction occurred in the number of weekly users of cocaine. These data will allow policymakers to more effectively target resources towards the reduction of drug abuse and constitute a valuable resource for drug abuse epidemiologists who will conduct secondary analyses of the data base.

The Monitoring the Future Study, the second large-scale NIDA-funded epidemiological survey of drug use, was initiated in 1975 through a grant to the University of Michigan's Institute for Social Research. This survey measures drug abuse prevalence based on a sample of approximately 17,000 public and private high school seniors. It is conducted annually to monitor trends in drug abuse and related attitudes. Although high school seniors represent a very specific population, the findings pertaining to them are very important because young people are often at the leading edge of social change.

Drug Abuse Warning Network (DAWN): is a large-scale, ongoing drug abuse data collection system sponsored by NIDA. DAWN data are collected from a selected sample of emergency room and medical examiner facilities. The major objectives of the DAWN data system include: the monitoring of drug abuse patterns and trends, identification of substances associated with drug abuse episodes, and the assessment of health hazards associated with drug abuse. DAWN collects data from facilities located in 21 metropolitan areas throughout the continental United States and from a National Panel of emergency rooms. The medical examiner data are collected from 27 metropolitan areas.

Data from the DAWN system continue to show large increases in the adverse health consequences associated with the use of cocaine. Over the past five years, the number of hospital emergencies associated with the use of cocaine increased from 8,831 in 1984 to 46,020 in 1988. Between 1987 and 1988, the total cocaine emergency room mentions increased 33 percent from 34,661 to 46,020 mentions. The number of cocaine related deaths reported to DAWN more than tripled from 628 deaths in 1984 to 2,163 deaths in 1988.

Additional Datasets: In addition to the three primary datasets discussed above, NIDA uses many other datasets to measure the

nature and extent of drug use. In conjunction with the National Institute on Alcohol Abuse and Alcoholism (NIAAA), NIDA sponsors the National Drug and Alcoholism Treatment Unit Survey (NDATUS) and the State Alcohol and Drug Abuse Profile (SADAP). The 1987 final report of NDATUS included a new variable--the percentage of the active caseload (both drug abuse and alcoholism clients) who had been IV drug users at the time of admission. This variable is relevant for alcoholism clients as well as drug abuse clients because a proportion of primary alcoholism clients have a secondary drug abuse problem.

Other NIDA collaborative efforts include the National Adolescent Student Health Survey (NASHS), and support for the inclusion of drug abuse questions on several of the National Center for Health Statistic surveys, the 1988 National Maternal and Infant Health Survey (NMHIS) and the Hispanic Health and Nutrition Examination Survey (HHANES). NIDA also funded drug related questions on the Bureau of Labor Statistic's National Longitudinal Survey (NLS). In addition to collaborative efforts, NIDA uses other data bases where appropriate including Drug Use Forcasting (DUF) and the Worldwide Survey of Substance Abuse and Health Behaviors Among Military Personnel.

Drug Abuse Prevalence: NIDA's two major prevalence surveys showed increasing drug use from the early 1970's through 1979. Following that peak year, through the early 1980's, these surveys generally showed a reversal of the upward trend. The most recent (1988) National Household Survey on Drug Abuse indicates that about 72 million Americans aged 12 and older have at least tried illicit drugs or have used drugs nonmedically in their lifetimes. Among 18-25 year-olds, the age group with the highest prevalence of current drug use, the prevalence of nonmedical use of most licit and illicit drugs continued to decrease or level off. Increasing lifetime prevalence levels were found for persons age 26 and older, reflecting the aging of drug-using young adults.

A decreasing trend in current (past month) use of illicit drugs began in 1979 and accelerated between 1985 and 1988. Current prevalence rates for the population aged 12 and over for any illicit drug use decreased from 12 percent in 1985 to 7 percent in 1988.

Cocaine use is an exception to the general pattern of decline observed for drug use since the early 1980's. Nonetheless, there was a significant decline between 1985 and 1988 in the percentage of seniors who reported current cocaine during the past month. This trend is consistent with the downward trend seen in the household population, where past month users dropped by half.

Adverse Health Consequences: Despite the encouraging downward trends in prevalence, the adverse health consequences connected to substance abuse are increasing. The number of people admitted to emergency rooms following cocaine use increased over five times from 1984 to 1988. Furthermore, the number of people who

died following cocaine use more than doubled during the same time period. Emergency room care increased 1.5 times for heroin related incidents over the same time period. Even emergency room care for marijuana use has climbed 2.3 times. During a period of declining prevalence, some of the factors which contribute to increases in health consequences among people who continue to use are: increases in frequency of use, increases in dosage, changes in route of administration to more dangerous routes (e.g. smoking), the use of drugs in combination, and complications associated with long-term use and aging of the user.

Deficiencies of Data: In spite of the variety of data collection systems available to determine the nature and extent of the drug abuse problem, informational gaps remain. Large segments of the U.S. population are difficult to enumerate or to access because they are transient, homeless, institutionalized, chronically mentally ill, or precariously housed. Few studies have been done, but data from the Institute of Medicine's Homelessness, Health, and Human Needs Report suggest that persons comprising these "hidden" populations experience a greater prevalence of drug abuse and adverse effects from drug abuse than persons from the general household population. Furthermore, since some drug abuse behaviors (e.g., heroin injection) are relatively rare in the general population, they are difficult to estimate from the national prevalence survey of households.

Current data collection on the prevalence of drug use in States and metropolitan areas is not adequate to identify areas with unique problems. State survey data frequently are not comparable, and although the consequences of alcohol and drug abuse are widely known, mortality and morbidity rates and distributions of such consequences among all populations (general and at-risk) are not being systematically collected. For example, data on the extent to which alcohol and drug abuse are implicated in accidents, traumatic injuries, and other medical crises besides those explicitly involving overdoses are needed. One possiblity for addressing this informational gap might be to make toxicological testing routine for all patients admitted to short-stay hospitals and for the recently deceased due to intentional or unintentional injury, including automobile accidents. This could provide baseline data on the extent of involvement of these substances in deaths and years of potential lives lost in the U.S. each year.

Limited data indicate that the crack epidemic has affected infants and children of drug abusing women largely because many users are women in their child-bearing years. The tendencies of crack users to engage in unprotected and frequent sexual intercourse and the added risks that such persons may use other drugs intravenously, put these women and their fetuses and infants at great risk of AIDS. Research suggests that large metropolitan areas may be experiencing an epidemic of HIV-infected and cocaine intoxicated newborns being born to center city women. However, the nature and extent of these

problems across the nation, in both urban and rural areas, has yet to be determined.

New Data Collection Efforts: To address various informational gaps, NIDA has initiated several new data collection efforts and identified future activities to follow up those that are currently underway. Two efforts begun in the fall of 1989 are the Metropolitan Area Surveys Project and the In Utero Drug Exposure Survey.

The Metropolitan Area Surveys Project is a large-scale study of the prevalence, incidence, and consequences of drug abuse in the Washington, D.C. metropolitan area. Drug abuse data will be gathered and analyzed from households, elementary and high schools, hidden populations, drug treatment centers and medical and law enforcement agencies. One objective of the study is to demonstrate that a comprehensive data collection system can be developed and used for public health monitoring and resource management by local community, State, and Federal health care providers and policy decision makers.

An In Utero Drug Exposure Survey is a hospital-based study that will assess the extent to which babies are born physically drug dependent or suffering consequences because of prenatal exposure to drugs. It will acquire data on the prevalence of prenatal exposure to all major drug types, the temporal patterns of that exposure, and the demographic characteristics of both infants and mothers. Results from this study will yield information identifying women who are at risk of drug abuse during pregnancy, and will support policy formation and public health efforts to prevent and treat drug abuse as early as possible.

The Modified Household Survey is a modification to the sampling plan for the 1990 National Household Survey on Drug Abuse that will expand the sample and oversample several metropolitan areas. This will provide prevalence estimates by age group in these areas, allowing comparison of metropolitan areas with national and regional data. Also, in conjunction with the 1990 Household Survey, NIDA will conduct various methodological studies designed to improve the quality of the data as well as our ability to interpret it.

The DAWN system is undergoing a transformation to a probability sample for emergency departments at the metropolitan area and national levels. The new sample will allow NIDA to produce national, regional, and local estimates of drug abuse episodes that are representative of hospital emergency cases in those areas. Thus, computation of rates will be possible, as well as comparison of these rates among the different areas.

TREATMENT MEDICATIONS

There is currently an urgent need for a formal program that will

develop new medications for treating drug abuse disorders. The reasons for this are essentially two-fold: serious drug abuse is becoming an increasing menace to the orderly functioning of society, and intravenous drug abuse is the major conduit of transmission of HIV infection to the heterosexual populations and to neonates.

In the past, the development of new pharmacotherapies for the treatment of drug abuse has suffered from a lack of interest by the pharmaceutical industry and a lack of clear federal committment to the organized, ongoing search for new treatment compounds; to programs for preclinical evaluation; or to systems to clinically evaluate promising medications. To redress this situation, NIDA has established a program to develop treatment medications. A Medications Development Task Force was created in 1988 to coordinate all activities, and funds provided by the Anti-Drug Abuse Act of 1988 have permitted NIDA to double its medication development efforts.

The program focuses on innovative approaches to drug abuse treatment and on improving already established modes of therapy. Efforts will be made to develop appropriate therapeutic agents for abused drugs other than narcotics. Particular emphasis will be given to cocaine and heroin. Full utilization will be made of animal models of addiction, and treatment regimens will be based on these results. Attempts will be made to modify fundamental brain processes involved in drug tolerance and dependence, and to delineate mechanisms underlying the reinforcing effects of drugs; to fully use knowledge about the structure-activity relationship of drugs; and to apply new knowledge from the field of molecular biology to the treatment of drug addiction.

Knowledge of the genetic mechanisms controlling the regulation of neurotransmitters may enable scientists to develop compounds that will nullify the effects of drugs without themselves being addictive. New medications can be developed that combine the best features of today's therapies--replacement and antagonism--in a single capsule. Most importantly, the ability to modify brain chemistry should enable the development of therapies that will reduce the "craving" for drugs.

Focus on Developing Medications

Previous drug abuse research has provided fundamental insights into drug-receptor interactions, the structure-activity relationships of drugs and the brain, and mechanisms underlying neurotoxicity. With this information and the use of state of the science technological advances in molecular biology and neural imaging techniques, NIDA is proceeding to develop pharmaceuticals that:

- Reduce the craving for abused drugs
- Block the subjective and toxic effects of abused drugs
- Moderate and/or eliminate the withdrawal effects of abused

drugs
- o Substitute for abused drugs with less toxic effects
- o Prevent (in special circumstances) the initiation of drug addiction.

Treatment of Opiate Addiction

Three pharmaceuticals show immediate promise of offering clinical utility; their development is NIDA's highest priority.

LAAM: An immediate goal is to make the drug, LAAM, available for treatment of intravenous heroin addiction. LAAM is a long-acting narcotic agonist drug with some unique advantages over methadone. LAAM need only be taken 3 times per week thereby decreasing visits to the clinic and breaking the daily drug-taking cycle. LAAM has a long, smooth duration of action and does not produce the "buzz" common to many narcotic agonists. It should have less potential for street abuse than methadone and so diversion should be less of a problem. Some clinical trials of LAAM have been completed. A sponsor who will evaluate the available data, obtain a NDA (new drug application), and, if the data are sufficient, who will market the drug, is being sought.

Buprenorphine: This drug is in an earlier stage of development than LAAM and still requires clinical trials. In addition, the formulation that will be most successful in clinical use has yet to be determined. Buprenorphine given sublingually shows great promise in suppressing heroin use among dependent intravenous heroin users. It appears to have some degree of abuse potential of its own, however, and cannot be dispensed for take-home use without some risk of misuse and illicit diversion. To overcome this liability, buprenorphine will be formulated to incorporate naltrexone or naloxone and binders to curtail subcutaneous and intravenous use of the preparation. Also, a formulation that will allow clinic personnel to know that the dose administered at the clinic is absorbed is being sought.

Depot Naltrexone: A third immediate priority involves the development of a depot preparation of the narcotic antagonist, naltrexone. Depot preparations are body areas (usually under the skin) from which solutions of stored medication can be distributed. Advantages to this form of administration are that patient compliance is ensured and fewer trips to the clinic are needed. Naltrexone has already been approved for such use but a sustained release (constant amount released with time) formulation should offer significant therapeutic and compliance benefits. A timed release formulation that will release medication at regularly scheduled intervals is now being developed. In addition, a triggered release formulation that will release medication only when stimulated by an illicit drug is envisioned for the future. It is anticipated that clinical trials of a marketable depot preparation can begin in mid-1991.

Cocaine Treatment

Treatment Medications: Many of cocaine's effects are mediated by the neurotransmitter dopamine. Some of the effects that underlie its euphoriant and addictive properties appear to be modulated through a specific type of dopamine receptor called D1. A variety of compounds that block the actions of dopamine at these D1 receptors have recently been discovered and are being studied to determine their possible therapeutic uses in treating cocaine addiction.

Studies of several already approved and marketed agents--e.g., calcium channel blockers, tricyclic antidepressants, dopamine agonists, and dopamine reuptake blockers--are underway to assess their therapeutic potential in treating cocaine addiction. Data exist for each of these categories that suggest some clinical utility in cocaine users. However, the question of the appropriateness of which medications, at which doses, under which circumstances and for which types of cocaine users is still poorly understood. Indeed, it is not yet certain that the benefits of using any particular drug are so well established as to justify its clinical use.

Cocaine Cardiotoxicity

In addition to finding treatment agents for cocaine abuse, NIDA will also attempt to develop pharmaceuticals that can prevent some of cocaine's toxic effects. Data suggesting that calcium channel blockers (common antihypertensives) may be useful in preventing cardiotoxicity are available from animal studies. Work with large non-primates (e.g. dogs) and larger primates, as well as studies of biochemical markers of cocaine blockade are needed to better define the circumstances under which these and other agents might be used. Because some calcium channel blockers are already approved by the FDA, it may be possible to develop one of these agents for an NDA within three to five years.

Cocaine Craving, Reinforcing Effects, and Withdrawal

Data indicating that calcium blockers alter the reinforcing effects of cocaine have come primarily from a study in which cocaine-induced euphoria was altered by pretreatment with nifedipine. Nifedipine, in its presently marketed form, is not well suited for the treatment of cocaine addiction because of its short duration of action. In addition, its cardiovascular actions make it difficult to increase the dose. It is thus necessary to study other available calcium channel blockers (e.g. verapimil, diltiazem, and a newly developed long-acting oral preparation of nifedipine); identify preparations best able to to block cocaine's effects, duration of action, side effects, etc.); and to test one or more of these in outpatient clinical trials.

The effects of calcium channel blockers on intravenous self-administration of cocaine by rats and the relationship of plasma

levels of calcium channel blockers on cocaine's reinforcing actions will be studied at the preclinical level. The administered dose of cocaine and of each available calcium channel blocker will be systematically varied to permit inferences about the capacity of the compounds to block cocaine's reinforcing effects.

Clinical researchers propose to expand present efforts and study the available calcium channel blockers and dopaminergic agonists in volunteer inpatient subjects with past histories of cocaine dependence. The paradigm involves administering a candidate calcium blocker or dopaminergic agonist followed by a challenge dose of cocaine while measuring subjective, physiological, and electroencephalographic variables. Human subject approval has already been obtained to study bromocriptine (a dopaminergic agonist) and the calcium channel blockers diltiazem, verapamil, and nifedipine. Since blockade of cocaine effects is likely due to CNS actions of calcium channel blockers, methods are being sought to identify the time course of the CNS actions of these agents. In addition, effects of some of these same agents on cocaine's reinforcing actions suggest that they may reduce craving during cocaine detoxification. Theoretically, this can reduce the time required for in-patient treatment. Current work on cocaine withdrawal will be expanded to include double-blind studies of the effects of the described medications on the intensity of cocaine craving during withdrawal. Pilot studies will be conducted at the outpatient clinical level of the medications emerging from these in-patient clinical efforts.

Animal Models of Cocaine Self-Administration

Efficiency in developing any treatment agent requires a sensitive animal model to use for testing of new compounds. NIDA researchers have developed animal self-administration models specifically for this purpose. Three aspects of cocaine addiction will be modeled:

Reward Value of Cocaine: In order to determine the magnitude of the reinforcing nature of cocaine, the point at which an animal will no longer work for drug administration will be determined.

Drug Craving: Craving will be measured by using an extinction procedure following long-term drug self-administration. The resistance to extinction (the amount of work after reward stops) will be taken as a measure of the desire to obtain the drug.

Relapse: Once cocaine self-administration has been extinguished, the ease with which drug taking can be re-established will be taken as a measure of relapse.

The above measures will be made to estimate success of treatment. Once cocaine self-administration is established and the above parameters determined, the animals will be treated with a variety of new compounds, and the outcome evaluated and compared with

effects of medications used presently for treatment.

Treatment of Benzodiazepine Abuse

The development of flumazenil (RO 15,1788) as an agent to rapidly reduce physical dependence on benzodiazepines (BZs) will be pursued. There are probably more people physically dependent on benzodiazepines (BZs) than on opioids. Since high doses of BZs are now a mainstay in the treatment of phobia it is likely that this situation will persist. NIDA scientists have developed a protocol (now being carried out at the preclinical level) which examines the receptor resetting properties of BZ antagonists. Just as the use of naltrexone in methadone dependent subjects has been shown to shorten the time needed for completion of in-patient opioid withdrawal, it is hoped that comparable advances can be made in treatment of BZ withdrawal using BZ antagonists.

Treatment of Chronic Pain

A major problem in studying how opiates affect the nervous system is that there are at least three sets of opiate receptors. Many narcotics will have some effect on all of these receptors, even if they bind most strongly to one. This makes it difficult to determine the precise location of a narcotic's action in the brain that is responsible for a specific effect, e.g. euphoria, dependence, analgesia, or respiratory depression. Because of this, NIDA researchers have devoted considerable effort to develop opiate agonists and antagonists that are highly selective for particular types of opiate receptors.

A breakthrough has been made recently in obtaining a highly selective series of delta opioid receptor antagonists, naltrindole and its analogs, which are based on the "message-address" concept. This concept explains the activity of bivalent ligands (a class of compounds with two binding sites): theoretically they bind in such a way that one-half of the ligand determines which receptors the ligand will bind (the "address"), while the other half determines the pharmacological response (the "message"). Naltrindole and its analogs will open the door to many in vivo studies.

This finding holds much promise for future research because it indicates that it may be possible to alter opioid peptide antagonists selectively, in a predictable way, by altering the address component of the peptide. If so, it should be possible to develop a range of highly selective substances useful in studying how narcotics work in the brain and in designing potent analgesics with fewer unwanted side-effects.

Receptor Binding Studies and Drug Development

Receptor binding is a commonly used, powerful tool in medication development. It has become an indispensable adjunct to clinical studies. There are several ways that we propose to use receptor

binding. One is to determine the potency of a drug at its receptor. This can provide some initial estimate of dose which can be compared to known medications. Moreover, any metabolite can be tested for activity in simple binding assays.

Receptor binding can distinguish agonists from antagonists and is relevant to any of the above mentioned projects on cocaine, opiates, benzodiazepines, PCP, etc. It can also be used to determine the pharmacological profils of any interesting drug. Drugs are rarely clean, i.e. bind to only one receptor. Cocaine, for example, binds to several sites in brain, but available evidence suggests that only one of these sites is related to drug dependence. All potential medication candidates will be subjected to a battery of 30 or so receptor binding assays to provide a complete picture of the pharmacological activity of the drug.

Also, a detailed "picture" of the receptor site can be obtained by structure activity relationship analysis. For example, the cocaine receptor is not well understood and a detailed structure activity study would provide a description of the shape of the active site of the receptor. This is fundamental to any rational design of a new agonist or antagonist. The chemical compounds needed for such a study are either already available or are being synthesized. Structure activity studies for the PCP and cocaine receptors are currently being developed.

Clinical Trials

Once new chemical entities are identified as having therapeutic potential, they must be shown to be free of significant toxicity before being tested in humans. At least five such candidates will be available in 1990 for toxicity and carcinogenicity testing.

In 1989, human clinical trials were initiated in pharmaceuticals already tested for toxicity. These include buprenorphine, and carbamazepine, an anticonvulsant that has shown promise in reducing cocaine craving in early clinical trials. Other agents currently being evaluated for use in reducing the craving for cocaine include amantadine, bromocriptine, and flupenthixol. It is likely that these dopamine agonists, as well as new compounds with similar activity, will be more widely tested alone and in combination.

Also planned are clinical trials of monoclonal antibodies for the detoxification of acute PCP overdose. Monoclonal antibody therapy may be useful in treating other forms of drug addiction and will receive additional attention from NIDA. Finally, ongoing research dealing with genetic control mechanisms of opiate receptors and endogenous opiate-like substances hopefully will yield new approaches to the treatment of narcotic abuse.

Treatment Research Units

NIDA has established a series of Treatment Research Units to coordinate and expedite the process of medications development and to serve as national centers of excellence in drug abuse treatment. These units will allow for rapid testing of new treatment compounds either by NIDA or the private sector. Because these units will supply unique clinical expertise, leading pharmaceutical companies will be able to focus some of their internal scientific talent on innovative approaches to drug addiction treatment.

As a first step NIDA will develop criteria for a pharmacotherapy for cocaine abuse; these will be matched against compounds coming through the screening program. Compounds that meet some, but not all, of the criteria would be subjected to structure-activity analysis. In this way, new pharmaceuticals that conform specifically to our criteria could be created.

Not only will these units help to change the priority given to the pharmacotherapy of abuse, but the training of clinicians and scientists skilled in pharmaceutical development procedures will be substantially increased. Experience has shown that these individuals will continue this line of study in other settings.

Continuing Accomplishments 1989

Treatment of Cocaine Addiction with Flupenthixol: NIDA grantee Frank Gawin and colleagues reported in the April 1989 Archives of General Psychiatry that the medication flupenthixol may possibly be highly effective for the treatment of crack cocaine dependence. Flupenthixol is used to treat depression and schizophrenia. In this open label, open ended study, ten outpatients with a history of severe treatment refractory crack addiction were administered depot injections of flupenthixol decanoate. Side-effects were minimal, and the patients experienced a rapid, marked reduction in cocaine craving and use, as well as an amelioration of withdrawal syptomatology. The investigators theorize that the therapeutic mechanism of action relates to alterations in the neurotransmitter dopamine, believed to be prominently involved in the development of cocaine addiction. These scientific findings are quite preliminary and will require replication in a larger, double-blind, placebo-controlled study, which will commence shortly. If a similar therapeutic effect is found, this will be the first proven, successful treatment for crack addiction.

PAIN AND ANALGESIA

Opiates are the most potent analgesic agents available today. Because opiates are one of the most addicting classes of drugs to which a strong physical dependence can develop, their use is not without some negative and potentially harmful side-effects. NIDA has a major interest in understanding the neural mechanisms

responsible for pain processing and opiate analgesia (pain relief) and in understanding the mechanisms of opiate addiction. Moreover, NIDA is striving to develop a therapeutic rationale of managing pain more effectively, while reducing the potential for abuse and the development of physical dependence.

The Production of Pain: The subjective experience of pain results from a series of complex electrical and chemical events along the pain pathways. The first event in the generation of pain is the stimulation of free nerve endings in the peripheral tissue. A painful or noxious stimulus activates the pain receptor (nociceptor), initiating a sequence of neural impulses that travels along its axon and terminates in the spinal cord. There are three types of pain nerve fibers that channel pain information to the spinal cord. C-fibers--small-diameter, unmyelinated fibers--conduct neural impulses slowly; A-delta fibers--larger diameter, myelinated fibers--conduct neural impulses more quickly; and A-alpha fibers--the largest diameter, myelinated fibers--are the fastest-conducting. The majority of A-alpha fibers transmit light-touch information rather than pain.

Anatomy of the Ascending Pain Pathways: The ascending pain pathway originates with the pain receptor in peripheral tissue and ends in the brain, in either the thalamus or cerebral cortex. The peripheral sensory receptor and axon, or first-order neuron, extends to the structure at the very top (dorsal horn) of the spinal cord. The second-order neuron links the dorsal horn of the spinal cord with the thalamus (passage in the brain to the cerebral hemispheres). The third-order neuron extends from either the thalamus to the cerebral cortex or to the limbic system.

There are two major chemical transmitter systems involved in pain transmission. Substance P (SP) is a peptide, originally discovered in the intestine and later in brain, found in A-delta and C fibers, and in dorsal horn neurons. SP is the neurotransmitter in the first-order neuron. The other major transmitter system involved in pain modulation and reduction are the endogenous opioid peptides. Enkephalins bind to certain opioid receptors in brain, produce analgesia, and are ubiquitous in the nervous system. Endorphins have analgesic properties but are confined to the hypothalamus and pituitary. Dynorphin, a potent analgesic, has been isolated from the posterior pituitary and several other brain regions.

The Descending Inhibitory Pathway: An interplay exists in the dorsal horn of the spinal cord between the "pain-facilitating" substance P and the "pain-inhibiting" enkephalin systems. This interplay occurs from an interaction of ascending sensory messages balanced by a descending inhibitory influence that forms a negative feedback loop. The first-order neuron is activated and transmits its message to the second-order neuron via SP. On the axon of the first-order neuron are opioid receptors that when activated, inhibit the release of SP thus reducing the

transmission of pain messages. These opioid receptors may be activated endogenously by enkephalins or exogenously by analgesic drugs. Failure of this negative feedback system to operate may account for some of the chronic pain syndromes that afflict a large clinical population.

Problems of Addiction Associated With Treatment for Chronic Pain: Given the analgesic potency and addictiveness of opiates, the potential for developing an addiction to an opiate analgesic is great, particularly if high doses are needed for long periods of time. NIDA has been studying the mechanisms of opiate dependence, tolerance, and withdrawal in hopes of developing more effective analgesics with less abuse liability, and recent preliminary research is showing that effective pain-relieving doses of opiates are not always addictive in pain patients.

In the absence of any exogenous opiates, the central nervous system responds normally to endogenous opioid peptides by inhibiting neural activity in the postsynaptic neurons. In the case of prolonged exposure to excess amounts of exogenous opiates, e.g. morphine, the normal function of the nervous system becomes altered; endogenous peptides are not produced and used in a "normal" manner. But, because of the presence of exogenous opiates, the inhibitory postsynaptic effects still exist.

When the external source of opiates is removed, however, the normal condition of endogenous opioid neurotransmission is not reestablished until the nervous system resets itself. Decreased neurotransmission is thought to be responsible for the clinical manifestation of the opiate abstinence syndrome, which leads to a variety of symptoms strong enough to compel the addict to return to drug use.

Accomplishments

Agents Given Cerebrally and Spinally for Persistent Pain: The aim of this project is to examine the role opioids might play in the alleviation of persistent pain. Using an animal model designed to study chronic forms of pain, it was found that a kappa opioid receptor agonist had analgesic properties, whereas a delta opioid receptor agonist, had no effect. This study also showed that the central processing of chronic pain is different from acute pain.

Opioids and Desensitization to Substance P in the Spinal Cord: In another study investigating chronic pain, prolonged exposure to substance P resulted in a desensitization to its effects. This desensitization is influenced by an opioid system that is activated by the interaction of SP metabolites with receptors different from the SP receptors controlling pain, thereby desensitizing the system to SP. The SP metabolite fragments interact directly at mu-opioid binding sites suggesting a novel mechanism for analgesic effects.

Histaminergic Mechanisms of Analgesia: Research findings have revealed that nonopiate substances are important in the mediation of analgesia: nonopiate-induced analgesia (NOIA). NOIA is produced at higher pain thresholds than opiate-induced analgesia, and neither tolerance nor cross-tolerance develops. Histamine seems to be the primary mediator involved in NOIA. From this research, the potential for a new approach to pain management arises.

The Pharmacology of Acupuncture Analgesia: Studies to understand the neuropharmacology involved in electroacupuncture analgesia have revealed that this method induces release of endogenous opioid peptides into the spinal cord. Low-frequency electroacupuncture stimulation resulted in enkephalin release, whereas high-frequency electroacupuncture stimulation induced dynorphin release. These findings reveal electroacupuncture as an effective technique to reduce pain and show that nonopioid neurotransmitters are important in pain processing.

Pain, Excitatory Amino Acids and Drugs of Abuse: Excitatory amino acids (EAAs) also play an important role in pain transmission. A specific EAA, NMDA (N-methyl D-aspartate), selectively excites pain neurons in the spinal cord; these effects are blocked completely by phencyclidine (PCP). Thus is likely that PCP influences analgesia by interacting with NMDA receptors in the spinal cord.

Spinal Release of Endorphins by Opioids: Studies on the descending pain-inhibitory pathway have revealed two separate pathways that use epsilon and mu opioid receptors. The epsilon-receptor system is activated by beta-endorphin. This results in the release of enkephalins in the spinal cord which produce analgesia. The mu-receptor system is activated by morphine, which produces analgesia by releasing serotonin and norepinephrine in the spinal cord. The epsilon-receptor system and the sites sensitive to morphine were found in different locations of the brainstem. This work provides clear evidence of more than one neuronal mechanism of action for the production of analgesia.

ETIOLOGY/PREVENTION

An understanding of the causal patterns and factors leading to drug abuse is a necessary prerequisite for attempting to control the behavior. Since drug abusers are a heterogeneous group, there are multiple pathways which may lead to substance abuse. Also, individuals appear to be differentially at risk for engaging in drug abuse and for developing dependence. An understanding of the various pathways and the factors which predispose or protect an individual from drug abuse is essential to the successful prevention and treatment of drug abuse.

Much of the early research that attempted to determine the risk

factors for drug abuse was based on retrospective self-reports of long established abusers with minimal independent verification; control samples, if used, were often poorly matched; and numerous studies adopted a correlational design which could not discriminate causes from consequences.

Drug abuse also can be viewed in terms of the social context in which it occurs. The same behavior may have vastly different significance and be associated with different causal factors at different points in time and for different social segments. This affects the generalizability of the etiological information. The risk factors for drug involvement when the behavior is extremely rare and deviant may be quite different from those when the behavior is generationally normative. Additionally, the factors predictive of low level, infrequent use may be different from those predictive of greater drug involvement. Furthermore, neither of these patterns necessarily informs us about the risk factors for contemporary drug involvement.

In the mid- to late 1970s, the methodologic maturation of social and psychiatric research and an increasing federal role in research on drug abuse significantly enhanced the quality and utility of etiologic/risk factor research. NIDA, making a long term investment of resources, supported methodologically sophisticated longitudinal multifactorial studies which resulted in much of the risk factor information available today.

NIDA's etiology research program supports a variety of research programs which focus on the origins of drug abuse answering questions about the multiple causal patterns and factors leading to and facilitating drug abuse. A primary goal of the Institute's etiologic research is to develop the necessary information, theories and methodologies to identify individuals vulnerable for drug abuse and to specify conditions that act as cues to become involved with drugs. An understanding of the etiology of drug abuse will make it possible to determine the critical causal factors and the most effective targets of intervention. Another aspect of etiologic research relates to the consequences of drug use on the physical, psychological and social development of the drug user. Studies of this nature examine the developmental etiology of drug abuse, the developmental consequences of drug abuse, and developmental interventions related thereto. Issues regarding this latter area will be discussed under the Intervention section.

Vulnerability: Understanding of factors that predispose or protect an individual from drug abuse is essential to the successful prevention of drug abuse. Clarification of the etiology of drug abuse and dependence requires recognition of vulnerability and being at-risk. Vulnerability refers to the fact that individuals are differentially predisposed for engaging in drug use and for making the transition from drug use to drug dependence and needle use. Being placed at risk refers to those conditions or situations which act as cues for vulnerable

individuals to chose between using or resisting use of drugs.

NIDA is investigating vulnerability to drug abuse from several directions. The purpose of this behavioral and clinical research is to: (1) improve our understanding of genetic and environmental factors involved in the etiology of the disorder; (2) identify groups at high risk for the development of the disorder; (3) facilitate the development of programs effective in preventing the disorder in high-risk groups; and (4) improve efforts at treating the disorder by allowing etiological factors to be addressed during the treatment process.

Current research is focusing on:

- The heritability, mechanisms, and markers of biologically based factors;
- The physiological, biochemical and/or neurological correlates, mechanisms, and manifestations of inherited, congenital, or developed predisposing biomedical factors;
- Social, familial and environmental factors;
- The psychological, developmental, social, environmental and psychopathological factors and behaviors involved in the predisposition, initiation, escalation, maintenance and recidivism of drug abuse and dependence;
- Youth who are vulnerable to drug abuse and their involvement in anti-social and deviant behavior, educational deficiencies, alcohol and cigarette use, accidents, precocious sexual experimentation, and suicidal tendencies; and
- Prospective identification of early biological and behavioral markers that can be used clinically as valid diagnostic measures.

Etiology of Drug Abuse Among Ethnic Minority Youth: NIDA and the Office of Juvenile Justice and Delinquency Prevention (OJJDP) have an interagency agreement to develop and fund a research program on the etiology of drug abuse among ethnic minority juvenile populations. The NIDA-OJJDP initiative is developing a base of etiologic research concerning developmental, social, economic, familial, and cultural factors which may play a role in drug abuse and upon which prevention intervention strategies can be based. Of particular concern are culturally-related factors associated with drug abuse and the interactional effects of minority status, acculturation, delinquency, and drug use.

Human Development Studies: All major classes of drugs of abuse are known to cross the placenta and influence the development of the fetus, the course of pregnancy, and subsequent development. Yet little is known of the magnitude, mechanisms, and duration of

the direct effects of drugs on the fetus or of the effects of drug abuse at other stages of development. Theoretically, the younger the age of onset of drug use, the more pervasive and severe the consequences and disruption of the individual's development and education. Early onset of drug abuse in childhood and early adolescence and patterns of onset at later ages can also be an indicator of predisposing genetic, biologic, psychopathologic, or environmental risk factors. Findings indicate that the risks for initiating or escalating drug use and the consequences differ by age, gender, and health status--including increased vulnerability to the effects of drugs during adolescence, pregnancy, and at advanced ages. However, information is not adequate for fully assessing and quantifying risk status within sub-populations.

Research in human development, the neurosciences, and drug treatment research--and our experience in prevention research--supports the need for more focused studies on the direct and indirect effects of drugs on human development as a basis for designing more effective prevention and treatment strategies.

Improved instruments and methods are needed to assess neurobehavioral and developmental effects of exposure to drugs and to assess levels of risk. Clinically and culturally relevant instrumentation and intervention strategies for appropriate different ethnic-cultural and age groups need to be developed, and legal and ethical questions that exist in this type of research and that carry possible legal consequences in terms of right to privacy, child custody, school, employment, and misuse of records, need to be resolved.

NIDA's Developmental Studies Program includes several interrelated components. They include research on maternal drug abuse and prenatal/perinatal exposure to drugs; etiologic relationships among drug use, developmental stages and transitions throughout the lifespan; the development of health beliefs and practices; normal developmental drives associated with risk-taking behaviors; developmental psychopathologies predisposing toward drug abuse (hyperactivity, attention deficit and learning disorders, psychomotor impairments, hyperaggressivity, etc.); child rearing practices; child abuse and neglect; coping strategies; the role of drug use in problem behaviors such as delinquency, high risk sexual activity, and adolescent pregnancy. Developmental etiologic factors include biologic, genetic, psychiatric, behavioral and social vulnerabilities and prenatal exposure to drugs which can be the consequences of prior drug use by either self or the biologic parent.

Accomplishments

Component Report on Drug Abuse: The Component Report on Drug

Abuse authored by staff appeared in volume two of the DHHS Expert Panel Report on the Content of Prenatal Care released by the Secretary of Health and Human Services on Child Day, October 2, 1989. This encyclopedic report on the effects of eight classes of abused drugs on the fetus and mother reviews recent findings from clinical studies.

Prenatal Substance Abuse in Adolescents: One study of adolescent single mothers in Seattle--the first field study to focus on this particular population--investigates interrelationships between pre-pregnancy drug use and abuse, early pregnancy, child-bearing, post-pregnancy patterns of drug use, unprotected sexual activity, repeat pregnancy, and mother and infant development. Preliminary data promises that the study will offer significantly enhanced intervention strategies for the target population.

INTERVENTION/PREVENTION

Prevention research consists of two parallel and interdependent lines of research. One line of research, etiologic, is to define factors associated with the initiation and progression of drug abusing behaviors. The second line of research is to develop and assess intervention approaches to intercede in the onset and progression of drug use and associated anti-social, anti-health behaviors.

Briefly, the progression of drug abusing behaviors consists of: (1) an initial vulnerability, (2) choosing to resist or use drugs when given an opportunity, and (3) escalation of drug use. Research related to defining this progression has been fruitful but further hypothesis-based studies are needed. The primary objective of prevention intervention is to prevent initial drug use and interrupt the progression to more intensive use of multiple substances. Two major research components need to be addressed: (1) assessments of the outcomes and impact of ongoing intervention programs, and (2) development of new/innovative prevention intervention strategies. Special emphasis should be given to:

- Interventions for high risk youth;
- Early interventions designed to prevent the escalation of drug use to dependency and associated anti-social and health problems;
- Developmental intervention programs designed to prevent developmental lags, disabilities and vulnerabilities resulting from drug use and fetal exposure to drugs; and
- Community-wide, comprehensive intervention strategies.

Objectives of prevention research include: (1) determining the efficacy and effectiveness of single component and comprehensive

prevention programs to change drug use knowledge, attitudes, and behaviors; (2) assessing models for diffusion, to the prevention field and general public, of scientific findings emerging from basic and intervention research; (3) testing the effects at the community level of drug abuse policies and prevention practices through process, outcome, and impact research and to assess the cost-effectiveness and cost-benefit of preventive interventions; (4) developing and testing theory-based interventions to reduce risk of pediatric and adolescent HIV infection and intravenous drug use and abuse; and, (5) developing advanced research methods, measures, and data analyses procedures appropriate for assessing the efficacy and effectiveness of prevention interventions.

Epidemiological, ethnographic, etiological, drug abuse liability, and health behavior research have all contributed to the development of intervention strategies to prevent drug use initiation and progression to abuse and dependency. This research, accumulated over the past fifteen years, has provided scientific information regarding the: nature and extent of drug abuse behaviors specific to drug initiation and dependency; consequences of drug abuse behaviors; protective and risk factors associated with the abuse of drugs; abuse liability of substances; factors associated with the performance of health promotion behaviors; and, the development and testing of theoretical models for strategies to alter and enhance behaviors to promote good health.

Initially, prevention programming in the health and drug abuse field focused primarily on teaching the perils of drug abuse. Although knowledge may form the basis of rational decision-making for specific actions, factual information is interpreted and processed within pre-existing experiential and belief systems of individuals. As a result, prevention intervention research has explored a variety of theoretical models, including values clarification, social learning, coping and other training skills. These models have been and continue to be tested for the prevention of drug abuse. Also, over the past ten years, NIDA sponsored research has generated valuable scientific data concerning the health risks of a variety of substances. These findings have been communicated to the professional research community through peer-reviewed publications, to the general public through the release of drug-related reports from the U.S. Surgeon General's office and repeated media coverage of the drug problem, and to the school age population through the implementation of objective and scientifically accurate drug information and education programs. Epidemiological trend data from the High School Senior Survey suggest that this prevention activity is having a positive effect on adolescent use of marijuana and cocaine.

Analyses of data from the National High School Senior Survey have shown a consistent downward trend in self-reported marijuana use since 1978. The latest survey also indicates a decline in

cocaine use. Recently, researchers from the University of Michigan have directly attributed that the ten year decline in marijuana use by high school seniors to the dramatic increase in the perception of risk of psychological and physical harm and the increased perception of personal disapproval associated with the regular use of marijuana on the part of high school seniors. The report indicates that though lifestyle factors such as truancy, religious values, or political beliefs are linked to individual differences in the use of marijuana, these factors do not explain the general downward trend in marijuana use since 1978. Rather, the researchers conclude that if the perceived risks of harm and personal disapproval associated with regular marijuana use had not risen substantially since 1978, the decline in use of this drug would not have occurred.

It appears that, over the course of time, adolescents gradually have begun to realize that the use of marijuana can result in significant physical and social consequences that are detrimental to their health and social acceptance. Preventive messages conveyed by the "system" and particularly by the peers of youth concerning the negative effects of marijuana appear to be consistent with the social experiences of high school seniors and may have prompted a significant change in their use of marijuana. Likewise, the recent downturn in reported cocaine use has been associated with an increased perception of risk of harm resulting from regular use, occasional use, and use of cocaine once or twice. For example, the reported use of cocaine within the past thirty days by high school seniors declined from 6.7 percent in 1985 to 3.4 percent in 1988, while the perception of harm resulting from the use of cocaine once or twice rose from 34 percent in 1985 to 54.2 percent in 1988.

While scientific knowledge of the efficacy of individual prevention programs is still evolving through controlled research, the general downward trends provide encouraging initial indications that appropriate and scientifically-sound drug prevention messages are effectively reaching a large proportion of our adolescent population.

Over the past fifteen years, extensive research has assessed the efficacy of specific drug prevention programs. Scientists at the State University of New York at Albany recently reviewed 143 adolescent drug education program evaluations that were published between 1972 and 1984. The investigators used a statistical technique called meta-analysis, which is used to combine and compare research findings from a number of different studies by transforming the reported data into a standardized metric called the effect size.

In analyzing these reports, the researchers identified five types of programs: Knowledge Only, Affective Education (self-esteem building, values clarification, etc.), Peer Education (combination of knowledge and peer leadership, peer teaching, and positive peer pressure groups), Knowledge plus Affective

Education, and Alternatives (wilderness training, personal competence development, etc.).

Of the five prevention program modalities tested, peer programs were found to be the most effective in obtaining clinically significant effect sizes on all outcome measures including increases in drug-related knowledge, negative attitudes toward drugs, and decreases in the use of cigarettes, alcohol, and other drugs. Peer programs are characterized peer participation in program planning and implementation. Peer programs frequently included training in drug refusal skills, and intra- and interpersonal development such as interpersonal communication, self-esteem building, anxiety reduction, coping skills training and the formation of personal competence and self-confidence.

In addition, the analysis revealed that Alternatives programs were particularly effective for high risk youth who were already having school problems, were using drugs to some degree, and who may be delinquent. Alternative programs are characterized by their focus upon providing youth community-valued and sanctioned activities that may counter the apparent appeal of drug use; these may involve the concepts of volunteerism, community service, entertainment, and employment opportunities. A second focus of Alternatives programs entials development of personal competence through the provision of basic education in reading/math, and job skills. Alternative programs also provide wilderness experiences that offer youth both the excitement and challenge of confronting and overcoming events in one's environment.

This review of 143 studies concludes that: most drug prevention programs can significantly increase knowledge concerning the negative effects of drugs; drug prevention programs that utilize positive peer groups can produce in the general adolescent population clinically significant increases in drug knowledge, anti-drug attitudes, and reductions in drug use in comparison to controls; and, that Alternatives programs produce positive drug-related effects comparable to those of peer group programs, particularly for high-risk youth.

Stages of Drug Use Onset and Progression: Drug dependency and addiction are progressively developing chronic health and social problems that encompasses eight stages of development. They are:

1) Non-use,
2) Initial Drug Use,
3) Experimental Use,
4) Occasional/Frequent Use,
5) Use as an Integral Part of Lifestyle,
6) Abuse/Dependency,
7) Recovery, and
8) Maintenance of Drug-free Lifestyle.

The term drug abuse prevention encompasses a range of activities

appropriate to the first five stages of progression. While some have viewed the scope of prevention as involving only the first two stages, i.e., the transition from non-use to initial or first time use, these are only the first two of five stages of drug abuse development that are within the purview of drug and alcohol prevention programs. Drug prevention programs implemented today at the State and local level go well beyond the restricted concept of primary prevention to include prevention activities aimed at youth and young adults who are moving through the stages of Drug Experimentation, Occasional/Frequent Use, and Making Drugs an Integral Part of their Lifestyle to the point of a medically diagnosed drug abuse problem. At that point, prevention as a health program concept ends and drug treatment, with its many therapeutic approaches, begins. Optimistically, treatment will eventually lead to recovery which can be maintained through rehabilitation and relapse prevention activities that an individual pursues after leaving treatment.

Comprehensive Drug Abuse Prevention Research: Etiologic research indicates that drug use onset and progression to abuse involves a variety factors that may make an individual vulnerable to drug use and abuse. Given the complexity of the problem, a promising approach provides multiple component, multiple level drug abuse prevention intervention strategies that focus simultaneously and systematically on the individual, family, peer group/peer cluster, and community (school, neighborhood, and workplace).

Risk and Protective Factors: In the late 1970's the U.S. Public Health Service provided increased attention to disease prevention and health promotion by utilizing the risk factor model as the basis for national health programs. Guided by the model, specific factors that place an individual at risk for disease are identified by epidemiologic and etiologic research and targeted for corrective action. Research also is initiated to identify factors that may protect an individual from the disease or health problem. Disease prevention and health promotion strategies are designed to either remove or reduce the intensity of the risk factor, lessen its potential adverse effects and develop or enhance those factors that may protect individuals from disease. The risk factor approach to disease prevention and health promotion has been the basis for a number of prevention initiatives involving, for example, cancer, HIV infection/AIDS, alcoholism, and drug abuse.

Drug abuse research has identified a variety of risk and protective factors that appear to be correlated with the drug abuse problem.

Etiologic research has provided a theoretical basis and empirical structure to our scientific understanding of the causes of drug abuse. Also possible preventive interventions that could be designed and tested were revealed. So far, research indicates that drug use, abuse, and progression involves multiple factors that can be grouped within four general clusters to include

factors that pertain to the individual, family, peer group, and the community (school, workplace, and the neighborhood). This body of research suggests that drug use and abuse does not have a single causal agent, but a variety of agents that collectively place individuals at greater risk of drug use and dependency.

Risk factors reported in the literature include:

Individual:

1) early use of a drug, (e.g. alcohol, cigarettes);
2) non-conventionality, inadequate social bonding and deviant behavior;
3) novelty or sensation seeking;
4) personality factors such as early signs of aggressive and or noncompliance behavior;
5) low religiosity;
6) low academic achievement;
7) psychological distress or depression;
8) low self-efficacy or self-acceptance;
9) inaccurate or mis-perceptions of the harmful consequences of drug use; and,
10) social approval/disapproval of drug use behavior.

Family factors:

1) a familial history of alcoholism and/or anti-social behavior;
2) parental and older sibling drug using role models;
3) ineffective parenting practices; and
4) lack of mutual parent-child attachment and warmth.

Peer factors:

1) the use of drugs by peers;
2) peer cluster influence through social interaction and conjoint development; and
3) peer social pressure.

Community factors:

1) availability of drugs and alcohol;
2) law enforcement practices pertinent to driving under the influence of drugs or alcohol;
3) price of alcohol and price/purity of other drugs;
4) minimum drinking age laws;
5) social/cultural norms and mores relevant to drug use; and,
6) social stress resulting from lack of economic mobility, poverty, and inadequate social support networks.

Research indicates that the greater the number of risk factors, the more likely drug abuse is present. Given these research findings, it appears that there is not one simple and single explanation as to why an individual may be vulnerable to drug use and abuse. Likewise, this literature suggests that less exposure to salient risk factors may protect youth against the use and abuse of drugs.

How best to design an intervention or prevention program? Given multiple pathways to drug use and abuse, the most effective prevention approach would use multiple components that address a number of risk factors within the context of the same program. These programs could focus upon the prevention of precursors to drug use/abuse, such as aggression, early problems with interpersonal relationships, oppositional behavior, and arrested or inadequate moral/ethical development, as well as risk factors that emerge after drug use has become more frequent, intense, and problematic. An integrated approach to building stronger social bonds to the family, positive peers, and community institutions, such as the school should be developed and tested within the context of comprehensive drug prevention. For example, a prevention strategy could provide at the elementary grades expanded opportunities to learn and succeed in school to develop essential academic skills through mastery learning techniques, and to receive positive and consistent reinforcement for learning gains. Comparable program activities could then be extended to higher grade levels through high school.

Since drug abuse is a progressive, chronic health problem with multiple pathways, it may be necessary to target specific, developmentally appropriate preventive strategies to each stage of drug use initiation and progression and to each category of risk influence; i.e., the individual, the family, and the community.

Researchers at the University of Washington are currently testing the efficacy of a comprehensive family, school, and peer-focused prevention program with students in grades 4-6. Students were exposed to instructional methods to enhance effective learning, cooperation among peers, and positive attitudes toward school. Children were also taught peer refusal skills to resist social pressure to use drugs. Parents were trained to increase their children's involvement in the family through productive roles and activities and to clarify and communicate family expectations about drug use by family members. Preliminary research results indicate positive outcomes on five theoretically-based risk factors for drug abuse. These include reductions in anti-social behavior, improved academic skills, increased commitment to school, reduced levels of alienation and poor bonding, and reduced school misbehavior. Also, the researchers report that reduced incidents of "getting high" on drugs at school appear to be correlated with the experimental teaching program.

Yale University researchers report preliminary positive effects of their social-cognitive approach to drug prevention with youth in the sixth grade. Experimental students were provided a decision making and skills development program initially in the sixth grade and again in the eighth/ninth and the tenth/eleventh grades. Parents of experimental students also received skills training. Results of the sixth and eighth/ninth grade student intervention suggest that students in the experimental program

showed a significant increase in decision making skills in comparison to controls and improved their peer resistance strategies. Parents demonstrated an increased ability to listen empathically to typical adolescent problem dilemmas and to use decision making facilitation skills. Relevant to drug use, the sixth graders in the experimental program reported a higher percentage of non-use and a lower percentage of regular use of cigarettes. This difference has persisted through the ninth grade. Analyses of drug use across the four years following the initial program experience indicate significantly lower levels of use by program students of tobacco and marijuana.

The character trait of sensation-seeking, appears to render one more vulnerable to drug-taking. Prevention research at the University of Kentucky indicates that high sensation seeking youth at the junior and senior high school level initiate greater use of marijuana, cocaine, alcohol and other drugs by ratios of 2:1, up to 7:1, compared to low sensation seeking youth as measured by the Zuckerman Sensation Seeking Scales. Research indicates that sensation seeking in humans may be biologically-based in that high sensation seekers tend to have low monoamine oxidase levels in blood platelets. Animal models are being studied to determine if novelty seeking behavior may involve the dopamine system (DA) in the brain, which overlaps with the same system involved in drug-seeking behavior relevant to the use of stimulants and opiates.

Summary: While prevention research is still being refined as a scientific discipline, NIDA-sponsored studies indicate that drug abuse prevention can result in meaningful changes in perceptions of drug-related harm, perceptions of social disapproval of use, drug knowledge, anti-drug attitudes, related social skills, and actual drug use.

Accomplishments

Midwestern Prevention Project: In 1984, NIDA initiated a drug and alcohol research program designed to promote multiple component, multiple level and comprehensive drug abuse prevention program research at the community level. As a result of that grant program, NIDA awarded a 5-year drug abuse prevention research grant to the University of Southern California to assess the efficacy of a comprehensive approach to drug abuse prevention. This Midwestern Prevention Project involves all the schools and communities comprising the Kansas City and Indianapolis Statistical Metropolitan areas. The research in Kansas City is of quasi-experimental design with 50 public middle and junior high schools matched on demographic characteristics and assigned to either a treatment or control condition. In Indianapolis, the research randomly assigned 59 schools to either treatment or control conditions.

Five interventions are being tested sequentially in each site, with one new intervention added each year. The first

Drug Testing and Laboratory Certification Guidance: As required by Public Law, NIDA published in the Federal Register, on April 11, 1988, The Mandatory Guidelines for Federal Workplace Drug Testing Programs, which includes the Scientific and Technical Requirements and Laboratory Certification standards for urine drug testing for federal agencies for achieving the goal of a drug-free Federal workplace. NIDA developed and published a "Urinalysis Collection Handbook for Federal Drug Testing Programs," and established a centralized collection contract to assist federal agencies implement the testing phase of their drug programs. The "Medical Review Officer Manual, A Guide to Evaluating Urine Drug Analysis," was published to provide guidance in the use of laboratory results to determine if drug abuse has occurred. Both the Collection Handbook and the Medical Review Officer Manual are available to the public through the National Clearinghouse for Alcohol and Drug Information and the 800-Workplace Helpline.

To enable federal agencies to implement their testing programs while the certification of commercial laboratories is occurring, temporary agreements with the Army and the Navy were established to provide interim testing services in Department of Defense certified laboratories. In conjunction with the Department of Transportation, NIDA has developed a chain-of-custody form for urine drug testing which is designed to be a standard for Federal agencies as well as for business and industry. The form has been pilot tested at The Department of Transportation and is expected to be published in final form in early 1990.

In response to private sector concerns on applicability of the Mandatory Guideline requirements for the regulated industries, and by businesses which want to use what is perceived as an excellent Federal model, NIDA convened a consensus conference in late 1989. Attendees included individuals from both the public and private sectors, from the laboratory community, and from Federal agencies. Based on scientific expertise and public concerns, NIDA will develop recommendations for the Department for revision of the Mandatory Guidelines.

NIDA provides extensive technical assistance to private sector employers on how to initiate the drug testing portion of a drug-free workplace program. This includes information on how to select and evaluate a laboratory and the necessity of using quality control specimens. Presentations have been made before trade associations and professional organizations.

National Laboratory Certification Project: As of August, 1989, 32 laboratories have been certified. Notification to the Federal agencies and the public of certified laboratories is provided through a regular schedule in the Federal Register.

To support the inspection phase of the laboratory certification program, a training course for laboratory inspectors was developed under contract to NIDA. This comprehensive course was

showed a significant increase in decision making skills in comparison to controls and improved their peer resistance strategies. Parents demonstrated an increased ability to listen empathically to typical adolescent problem dilemmas and to use decision making facilitation skills. Relevant to drug use, the sixth graders in the experimental program reported a higher percentage of non-use and a lower percentage of regular use of cigarettes. This difference has persisted through the ninth grade. Analyses of drug use across the four years following the initial program experience indicate significantly lower levels of use by program students of tobacco and marijuana.

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Summary: While prevention research is still being refined as a scientific discipline, NIDA-sponsored studies indicate that drug abuse prevention can result in meaningful changes in perceptions of drug-related harm, perceptions of social disapproval of use, drug knowledge, anti-drug attitudes, related social skills, and actual drug use.

Accomplishments

Midwestern Prevention Project: In 1984, NIDA initiated a drug and alcohol research program designed to promote multiple component, multiple level and comprehensive drug abuse prevention program research at the community level. As a result of that grant program, NIDA awarded a 5-year drug abuse prevention research grant to the University of Southern California to assess the efficacy of a comprehensive approach to drug abuse prevention. This Midwestern Prevention Project involves all the schools and communities comprising the Kansas City and Indianapolis Statistical Metropolitan areas. The research in Kansas City is of quasi-experimental design with 50 public middle and junior high schools matched on demographic characteristics and assigned to either a treatment or control condition. In Indianapolis, the research randomly assigned 59 schools to either treatment or control conditions.

Five interventions are being tested sequentially in each site, with one new intervention added each year. The first

intervention is mass media which is used each year of the project to heighten community awareness to the drug abuse problem and to introduce the new intervention being implemented by the program. During the first year, the project introduced a school-based peer resistance program called STAR (Student-Taught Awareness and Resistance) which focuses on the psychosocial consequences of drug use. Other interventions include: parent/family drug education and organization, community organization activities through creation of a drug council or task force, and efforts to change health-related policies in the community.

Results from the first year of the Kansas City project, reported recently in the Journal of the American Medical Association, indicate that sixth and seventh grade students in the program report significantly lower levels of alcohol, cigarettes, and marijuana at one year follow-up than students in the comparison condition. Preliminary, yet unpublished follow-up research indicates that these initial differences are maintained over the following three years and that the positive effects of the program may extend to the use of cocaine as well.

Persuasive Communication Techniques: A final area of progress involves the study of persuasive communication techniques appropriate for both drug prevention information/media campaigns and public education programs, particularly those focused upon high-risk individuals, such as high sensation seeking youth. Research suggests two categories of adolescents who may be most amenable to change evoked by targeted interventions include high sensation seeking non-users of marijuana, to prevent drug initiation; and low sensation seeking users of marijuana who may be quite open to messages that argue against further drug use. Current research is assessing the efficacy of professionally developed anti-drug prevention media messages tailor made for sensation seeking adolescents.

TREATMENT RESEARCH

An increase in illicit drug use in the 1960s created a need for research to understand both the phenomenon of drug abuse and the factors involved in its treatment. Thus, during 1969-1974, the NIDA-sponsored Drug Abuse Reporting Program (DARP) data system tracked nearly 44,000 clients at admission, during treatment, at discharge, and at post-treatment follow ups. This research was the first systematic national outcome research program that demonstrated the efficacy of treatment for drug abuse.

A need for continuing research in treatment outcomes led to a second national study of drug abuse treatment, the Treatment Outcome Prospective Study (TOPS). In TOPS, data were collected on some 11,750 clients admitted to treatment during 1979-1981. Given then increasing evidence that many drug abusers had serious psychological problems, TOPS sought in a limited way to address the influence of psychopathology on treatment outcomes.

The DARP and TOPS research, and smaller scale studies, showed that treatment effectively reduces drug use and has a positive impact on outcome criteria such as criminal activity, employment, and depressive symptomatology. The research showed that while pretreatment level of drug use and of criminality are good indicators of treatment outcomes, demographic and socioeconomic variables do not account for much of the difference in treatment outcomes.

Recent emphasis has been placed upon the concept of impairment as a prognostic indicator of treatment outcomes. "Impairment" is assessed on the basis of: the severity of psychological disturbance in clients admitted to treatment; the degree to which external problems (e.g., legal problems or inadequate job skills) impede treatment success; and the degree to which impairment is related to or independent of the client's substance abuse. This measure may prove valuable in optimizing treatment outcomes.

One of the most significant variables affecting treatment outcome is the length of time in treatment. As research has demonstrated that positive outcomes are directly related to increased time in treatment, studies designed to improve client retention have assumed increasing urgency and priority.

Key areas of treatment research include medications development, co-morbidity, psychotherapy, relapse prevention, learning factors, and the treatment of criminal justice clients.

Pharmacological Aspects of Drug Treatment Research

Methadone and naltrexone are the pharmacotherapies most widely used in treatment for opiate abuse. Other pharmacological interventions under investigation for opiate abuse include clonidine, buprenorphine, and LAAM (levo-alpha acetylmethadol). Chemical interventions being investigated for treatment of cocaine abuse include tricyclic antidepressants, dopamine agonists, and dopamine blockers.

Methadone: Methadone maintenance is the primary pharmacological approach used in treating opiate addiction; currently about 100,000 clients are seen yearly in methadone treatment. Methadone is an orally-administered synthetic opiate that can substitute for heroin. When administered daily, methadone allows the addict to function normally without fear of opiate withdrawal symptoms. While heroin addicts may reduce use immediately and dramatically upon enrollment in methadone treatment, success is ultimately reflects length of stay in treatment. Longitudinal studies of opioid users in treatment consistently show that methadone maintenance treatment has better rates of retention, and outcomes that are equal to or more favorable than other modalities.

Naltrexone: Naltrexone, a synthetic narcotic antagonist available by prescription since 1984, prevents detoxified heroin addicts from experiencing the euphoria of intravenous narcotics and protects them from physiological re-addiction to opiates. Although patient acceptability has generally been disappointing, recent studies indicate that women and economically advantaged men remain on naltrexone for longer periods of time, participate more regularly in outpatient aftercare programs, are less likely to relapse, and appear less emotionally disturbed at the end of treatment than others who have been studied.

Clonidine: Commonly used to manage hypertension, clonidine provides a non-narcotic regimen for detoxification from opioid drugs. Clonidine has been studied in combination with naltrexone for rapid opioid detoxification. Due to side effects, however, patient acceptability has been low. A transdermal route of administration that could last up to a week, possibly increasing patient acceptability while decreasing unpleasant side effects, is being studied.

LAAM and Buprenorphine: Two promising agents are still at the investigational. The medication LAAM is similar to methadone but longer-acting, requiring only a three-times-per-week dosing. Buprenorphine, a mixed agonist/antagonist agent that blocks heroin and can be used like methadone for maintenance treatment, is less addictive, less euphoriant, and safer than methadone.

Pharmacological Treatment of Cocaine Abuse: Once viewed as a relatively harmless, mounting evidence shows that cocaine is possibly the most addictive substance known. "Crack" cocaine, the smokable formulation, is cheap, potent, easy to use, immediately effective, and easily available. The addiction it produces is highly resistant to conventional treatment.

Research has focused on developing pharmacological interventions that will reduce craving and break the typical cycle of quick relapse following detoxification. Tricyclic anti-depressants (imipramine, desipramine, and doxipen) may normalize dopaminergic balance through re-uptake blockade, and are promising. Studies of desipramine at Yale University found it to be significantly better than lithium or placebo in prolonging initial abstinence and in decreasing craving. Two other early stage clinical trials of desipramine, however, have not reported a positive effect.

Another general class of compounds being studied are the direct dopamine agonists. These agents may mimic dopamine to counteract an hypothesized dopamine depletion induced by chronic cocaine use. Although L-Dopa, the primary treatment for Parkinsonism (which is characterized by dopamine depletion), does not appear to be effective, small clinical trials have suggested the efficacy of two other dopamine agonists, bromocriptine and amantadine--both used in Parkinsonism. They are currently being tested in several larger, controlled trials.

Small trials with two quite commonly used dopamine blockers, chlorpromazine and haloperidol (used widely to treat psychotic disorders) appear to augment withdrawal depression. However, one agent in this class, flupenthixol, has shown excellent results in an open trial. A larger, placebo-controlled study will be started shortly.

Among other agents being tested are two anticonvulsants: one, carmabazepine, which is similar in structure to imipramine, has shown some promise in a non-placebo-controlled study of about 20 patients. Valproate, a common anti-seizure medicine, is also being studied. New anti-depressants such as fluoxetine and sertraline, believed to work primarily on the serotonin neurotransmitter system that utilizes the chemical serotonin, are under consideration, as are the cardiac drugs verapamil and diltiazem, which seem to block the euphoric effects of stimulants. And a primate study which showed that buprenorphine also can reduce cocaine self-administration is being supported in preliminary clinical research.

Psychosocial Aspects of Drug Treatment Research

With the exception of heroin addiction, most abused drugs have no well-accepted, effective pharmacological treatment. Even when a pharmacological intervention is available, its applicability is likely to be limited. Individuals seeking treatment typically present with other problems: medical, psychological, such as depression or antisocial personality disorders; legal, family, or financial; and inadequate social or vocational skills. Regardless of whether drug use is a cause or result of--or is unrelated to these problems--research suggests that they must be treated in conjunction with the drug abuse disorder to reduce the likelihood of relapse. Often some form of psychosocial intervention is the primary, if not the only, treatment.

Thus, in addition to testing pharmacological agents, NIDA continues to support research to refine psychological and/or psychosocial therapeutic approaches. This research has attempted to identify antecedents to treatment, treatment processes (i.e. what goes on in treatment) and outcome. Areas of emphasis have included: interrelations between drug abuse and other biobehavioral disorders (e.g. eating disorders and stimulant abuse); problems of specific populations; special problems associated with particular agents (e.g. cocaine) or forms of drug abuse; and the interactions between behavioral, pharmacological and treatment variables.

Psychiatric Co-Morbidity: Psychiatric co-morbidity refers to the co-occurrence of drug abuse disorders with other psychiatric disorders. Patients with comorbid conditions are difficult to identify as well as to engage and retain in treatment. The drug abuse component may mask the mental illness, and vice versa. Also, the presence of one disorder tends to worsen the prognosis

for the other.

Research designed to test innovative treatments for these patients is expanding rapidly. "MICA" (for "mentally ill chemical abuser") treatment units are becoming more common in hospitals that see chronic patients. Experimental programs now underway include guided group therapy, didactic relapse prevention, outreach squads to identify these patients, and half-way and partial hospitalization models offering vocational and socialization training.

Relapse Prevention: Relapse--the resumption of drug abuse following a period of abstinence--is typical in drug abusers who have left treatment. Most relapse to illicit drug use occurs in the first 90 days following treatment. Since it appears that some subgroups maintain positive treatment outcomes and lower relapse rates, the determination of factors that increase vulnerability to relapse is an urgent area of study.

Program and client characteristics are being studied to learn how to optimize the effectiveness of treatment. Strategies include matching clients with programs, increasing the client's degree of engagement in treatment, and use of cognitive and behavioral techniques, such as contingency management, extinction of conditioned responses, and aversive conditioning. Social skills training, training treatment staff in relapse prevention, and aftercare/self-help groups. Many of the self-help groups now in operation are based on the 12 step Alcoholics Anonymous philosophy. While clinical impressions testify to the usefulness of such groups for the recovering drug abuser, such groups are difficult to study in scientifically controlled ways; such research is needed.

Although drug abuse counseling or psychotherapy is a major component of treatment, the relative effectiveness of these various types of therapies for particular categories of drug abusers has not been established. Several research efforts are currently in progress to address this issue.

Learning Factors: Environmental stimuli are influential in determining individuals relapse to drug use. Research in this area has suggested several promising treatment strategies. One entails counterbalancing the reinforcing aspects of drug abuse with social and pharmacologic punishment of drug use, coupled with social reinforcement of positive behavior. In contingency management, for example, the client agrees to achieve a specific treatment goal (e.g., abstinence) or forfeit something of value.

Research also has focused on identifying how withdrawal, craving, and euphoria become conditioned. Conditioned craving may occur independently of conditioned withdrawal responses. Ongoing work will determine whether extinction training, which has been found to work reliably in the laboratory, will generalize to the clinical setting.

Studies to Improve Treatment Effectiveness: In 1989, NIDA initiated several major research projects to improve treatment effectiveness, each of which is described briefly below:

Reducing the Risk of AIDS Through Treatment: The aim of this program is to demonstrate that improved drug abuse treatment are more effective than "treatment as usual" in reducing AIDS-risk behaviors; for example, intravenous drug abuse (opiate and/or other drugs) as well as types of drug abuse frequently involving unprotected sex in exchange for drugs or money to purchase drugs.

Treatment Outcomes: The Drug Abuse Treatment Outcome Study (DATOS) will collect and analyze treatment admission and outcome data over a five-year period. The study will follow 20,000 individuals coming into five treatment modalities in 50 treatment programs. Treatment modalities to be studied are short- and long-term methadone maintenance, short- and long-term residential treatment, and outpatient drug-free treatment. A sample of 4500 individuals chosen from those entering treatment will be interviewed approximately six months after leaving treatment to assess treatment outcomes. (Need to clarify 4,500 vs. 20,000 followed) As the first large-scale study of treatment outcome since the introduction of block-grant funding, DATOS will yield valuable information about the characteristics of individuals in treatment and the effectiveness of treatment as it presently exists.

Treatment and Maternal Care for Pregnant Women, Post-Partum Women, and Their Infants: Eliminating or reducing maternal use of illicit drugs by means of enrolling and retaining drug-abusing pregnant and post-partum women in drug abuse treatment may forestall the array of tragic consequences likely to affect their offspring. These studies will be designed to determine in what manner the provision of drug treatment, supportive services, and medical care benefits for drug abusing women and their infants influence drug use, physical health, lifestyle, family stability, and attitudes.

Treatment and Vocational Training in Exchange for Public Service: A fourth initiative consists of research demonstration studies to investigate the feasibility and efficacy of programs to provide drug abuse treatment and vocational training to clients in exchange for public service; i.e., as an alternative to requiring direct or third-party payment for treatment. Many drug abuse treatment programs now require clients to pay some portion of treatment costs. Since individuals seeking treatment often have financial and employment problems, this requirement may impose a barrier. Research has suggested that when the client must pay a portion of treatment costs, those with little or no income may forego treatment or engage in income-generating criminal activity to pay for treatment.

Accomplishments

Highlights of significant findings in drug abuse treatment research in the past year include:

Treatment Effectiveness: HIV seropositivity among high-risk drug users has been found to be related to the frequency of injections and needle-sharing contacts. In a study of methadone maintenance programs in three northeastern cities, a NIDA-funded investigator found treatment to be effective in reducing IV drug use and needle sharing among most male heroin addicts. At follow-up a year after the initial treatment, 82 percent of the 105 patients who dropped out of treatment had relapsed to IV drug use, while 71 percent of the 388 patients who remained in treatment had ceased IV use. During the three-year field study, the investigator found marked differences in the success rates of various methadone maintenance programs. Differences were not linked to patients characteristics, but to the length of stay in treatment, level of methadone dosage, and to variables reflecting the quality of treatment provided.

Long-Term Methadone Treatment: Dr. Mary Jeanne Kreek and associates at Rockefeller University determined that long-term methadone treatment not only is medically safe but that it appears to enhance immune function in intravenous drug abusers at high risk for AIDS.

Family Involvement in Recovery From Heroin Addiction: In an effort to improve outcomes for methadone patients, a 20-hour training program was developed to teach the family of methadone maintenance patients how to participate in the treatment process. Studies at the San Francisco General Hospital demonstrated that the program improves family relationships and reduces illicit drug use among the methadone patients.

Consequences of Reduced Access to Methadone: In 1984, Alameda County, California, instituted the "Two Year Rule," whereby methadone maintenance clients were subsidized by the county for no more than two years, at which time they could pay $200/month to stay in treatment or be detoxified from the program. NIDA-supported studies this policy found that in addition to the expected consequences of increased heroin use and needle-sharing (among those who were detoxified from treatment) and increased criminality (among those who wish to stay in treatment but could not otherwise afford it), the therapeutic relationship between counselors and clients eroded and the adaptive use by addicts of other publicly-funded social service and treatment agencies increased. Social services such as acute-care mental health facilities, sequential 21-day detoxes, and late or non-payment of fees, were ultimately more expensive to the county than subsidized methadone.

Naltrexone for Maintenance of An Opioid-Free State: In a study directed by Dr. Donald Wesson of Merritt Peralta Hospital (WHERE?), the addition of a moderately long-acting, orally

administered adjunct (naltrexone) to a recovery-oriented post-treatment program proved effective in maintaining an opioid-free state for a selected group of detoxified, formerly narcotic dependent persons. The research findings suggest that gender and socioeconomic status predict retention, relapse, and aftercare participation for naltrexone patients.

Family Involvement in Recovery: Clinical researchers at the University of Miami's Spanish Family Guidance Center developed a family therapy approach designed to overcome a family's resistance to begin or to remain in therapy by, restructuring family interactive patterns that interfere with treatment. More than 90 percent of the Hispanic families who participated in the family therapy volunteered to enter the family treatment portion of their adolescent's recovery program. Over 75 percent of the enrolled families successfully completed the treatment.

Comorbidity of Drug Use and Major Mental Illness: In a study of patients with both major mental illness and serious drug abuse, Dr. Anthony Lehman at the University of Maryland has preliminary findings of very high rates of drug abuse in patients with schizophrenia, affective disorder, and other serious psychiatric conditions. This finding of the often-underestimated prevalence of comorbidity underscores the need for skillful diagnosis and treatment of these patients.

Dr. Samuel Siris, at Long Island Jewish Hospital, is studying schizophrenic patients who have histories of drug abuse as well as severe depression. He has found a high co-morbidity of substance abuse with schizophrenia; also, anti-depressant treatment for the depressed patients, who are often "self-medicating" with illicit drugs, can lead to substantial clinical improvement.

In a study of psychiatric illness in cocaine abusers, Dr. Bruce Rounsaville, at Yale, has found increased major depression and anti-social personality disorder in patients, as well as a clearly elevated risk of these and other serious disorders in their first-degree relatives. Additional evidence of this pattern was found in studies by Dr. George De Leon; clients with a range of drug abuse problems who presented for treatment at therapeutic community programs were found to have unusually problematic psychological profiles. Self-reports of violent behavior, suicide attempts, and psychiatric hospitalizations indicate increasing prevalence of such problems among new drug abuse clients. Crack abusers were found to have significantly higher rates of suicide attempts than other drug abusers.

SERVICES RESEARCH

The demand for services research in the drug abuse field has intensified with the government's involvement in the financing, planning, and study of drug abuse treatment options. During the

late 1970s and early 1980s, NIDA mounted studies to: determine the efficacy of vocational and other rehabilitation strategies, therapeutic communities, and various forms of drug abuse aftercare models; assess service delivery by paraprofessionals; and understand and describe polydrug abuse. Since then, however, despite the pace of changes in the organization and delivery of drug treatment, the types of drugs used, and the extent of drug abuse and its impact on society, NIDA's investment in drug abuse-related services research has not grown commensurately, and knowledge regarding the relative quality, access, cost, and effectiveness of various drug abuse prevention and treatment modalities has advanced slowly.

The year 1989 was marked by calls for expanded attention to knowledge development regarding the efficacy, efficiency, organization, structure, delivery, and financing of the drug abuse treatment system. The Anti-Drug Abuse Act of 1988 authorized and appropriated significant new funds for services and services related research and mandated expanded state reporting requirements that will enhance acquisition of data for drug abuse services research. In the same law, the Congress required that NIDA develop a health services research plan to include questions about the efficiency and efficacy of different treatments for drug abuse. In recognition of the importance of services research in the drug abuse treatment field NIDA's Director established a Services Research Task Force to coordinate the development and integration of NIDA's services research planning activities. NIDA funded, at Brandeis University, its first Financing and Coverage Policy Research Center. This Center consists of a consortium of faculty and staff from Brandeis University, Harvard University, Boston University, and Health Economics Research, Inc. The Center is expected to play prominently in the development and execution of NIDA's services research agenda. Collectively these actions should help institutionalize and encourage the development of a sound drug abuse services research program.

In keeping with the resurgent interest in and opportunities for service systems research, NIDA is emphasizing studies in four areas: studies of populations at risk, treatment capacity, treatment effectiveness, and costs and coverage for treatment.

Populations at Risk: Who is using what kind of drugs? Who are the next generations of drug users? Who is in need of, and seeking treatment; who is not, and why? These are the questions that health services researchers attempt to address as they consider current and future need for treatment and prevention strategies.

Evidence of the need for treatment is available in data obtained from various sources, including the Drug Abuse Warning Network, the High School Senior Survey, the National Household Survey on Drug Abuse, and NIMH's Epidemiologic Catchment Area (ECA) study. As valuable as they are, none of these data sources provides

adequate information on the overall drug-using population. Certain high risk populations, such as high school drop outs, the homeless, and incarcerated individuals are excluded from the surveys; none permits analysis of State or regional variations in illicit drug use or treatment rates; and none of are focused on treatment. While the Household Survey, for example, suggests that the incidence of illicit drug use is stabilizing, other sources indicate that demand for treatment is increasing, in both the public and private sectors.

The best currently available national drug treatment utilization data are captured by the National Drug and Alcoholism Treatment Unit Survey (NDATUS) and the "snap shot in time" census reported by public sector providers participating in the State Alcohol and Drug Abuse Profile (SADAP). Again, however, limitations exist; both systems provide aggregate data, the usefulness of which is limited by incompatibilities among State sources and, in the case of SADAP, by the exclusion of private sector providers.

Approximately 850,000 episodes of drug treatment were delivered in the units responding to NDATUS in 1987 with 263,000 patients in treatment on October 30, 1987, up sharply from the 73,478 patients in treatment on September 30, 1982.

A number of factors confound our ability to predict current or future need for treatment including: the chronic and recurring nature of drug abuse; variations in the effectiveness of different treatments for different drugs and clients; and the rate of onset of treatable drug problems. Provisional estimates by the Institute of Medicine, combined with other sources, suggest that three to five million persons in the United States currently could benefit from drug abuse treatment.

Treatment Capacity: How many facilities, of what type, are currently providing services? What kinds of services do they provide? How are they staffed and financed? Is access to care adequate?

NDATUS contains reports on some 6,900 free-standing, hospital-based, and prison-based facilities. Treatment modalities in these settings include detoxification, outpatient drug-free, methadone maintenance, inpatient chemical dependency, and residential therapeutic. Facilities that offer drug only, or combined drug and alcohol treatment, comprise about 3/4 of the total number.

Excess hospital capacity during the past decade, combined with the growth of drug treatment insurance coverage, has contributed to the increase in the number of hospital units and beds devoted to drug treatment. The growth of free-standing units has been stimulated, at least in part, by increased private coverage of these services during the early and mid-1980s. Recently however, many large employers, insurers, and managed care providers have begun to seriously question the escalating cost of continued,

open-ended coverage of a variety of drug treatment programs.

Detailed knowledge about drug treatment capacity and treatment systems properties is limited. With the expanded data collection efforts on treatment capacity, clients in treatment, recidivism, and the financing of care required by the Anti-Drug Abuse Act of 1988, services researchers will be better able to describe and quantify the factors that affect treatment delivery system capacity in both the public and private sectors.

Treatment Effectiveness: What treatment works? Who benefits most from treatment? Is client:treatment matching effective? What treatment is best for specific drug addictions? What length of time in treatment works best?

Over the past decade, a variety of factors--e.g., the shift in Federal and State roles in funding treatment; changes in the organization and operation of individual treatment programs; and changes in both nature and use of illicit drugs and the treatment population--have had an impact on treatment effectiveness. As noted above, however, both services research methodology and the actual conduct of studies have failed to keep pace with the effects of these changes.

While methodological issues were addressed in both DARP and TOPS, such as the framing of "criterion questions" (i.e., indicators and criteria for successful treatment outcomes) and the development of alternative methods for measuring outcomes over time, little work has been published recently in this field. Other areas have lagged as well. For example, there are no universally employed operational definitions of what constitutes each of the different modalities of treatment; studies of treatment efficacy have not used standard definitions; research protocols have varied from site to site; and most studies of efficacy lack generalizability beyond the immediate confines of the treatment programs under study. Recent studies which have been conducted on only a few treatment sites lack the statistical power to support conclusions about the relative effectiveness of different treatments.

Furthermore, uniform outcome measurement standards have neither been developed nor widely adopted by the drug abuse services research field. A range of outcome measures, from abstinence to improved social function, has been suggested, but not agreed to by the field as a whole. While recent advances in drug testing (e.g., urinalyses) have proven beneficial for monitoring drug use, much work remains on the multi-dimensional aspect of drug abuse outcome research. Diagnostic methods and client:treatment matching require systematic research. Research is necessary, as well, to develop improved assessment protocols for the severity of drug abuse.

Also, little evaluation or assessment of quality of care has been undertaken in the drug abuse treatment field. While limited

research has been conducted on the "process" of drug abuse treatment have been undertaken, the more difficult task of assessing outcome and effectiveness criteria remains undone.

Cost and Coverage: Only limited research has been conducted over the past decade on the total national cost of drug abuse. The results of a few studies where insurance data have been pooled to assess the direct cost of drug abuse treatment suggest that drug abuse related health care utilization and costs--including those associated with AIDS and drug use--have been significantly understated.

As rising health costs continue to be analyzed, drug abuse, alcohol, and mental health related costs are reported to be increasing more rapidly than most other health care components. Insurers and employers are trying new approaches, such as managed care, to contain these costs, but little research has been undertaken to document the impact on costs or outcome of alternative insurance, financing, coverage, or managed care approaches to drug abuse treatment.

It has been well established in general medicine that financing and reimbursement policies impact the access, demand, and supply of health services. While it has been reported that treatment demand has affected the level and way in which payment for treatment is made, its impact on access and utilization of drug abuse treatment is only beginning to be studied.

It is becoming apparent that financing and reimbursement for drug treatment in the U.S. is two-tiered and has produced a two-tiered delivery system. Public providers derive about 90 percent of their revenue from public financing; private providers derive about 80 percent of their revenue from private financing mechanisms. Public sector revenues are almost 50 percent lower per client than private sector revenues. Although the two systems are not mutually exclusive, there appears to be minimal overlap between their patients and providers.

There has been a perceptible shift in the balance of financing between public and private sources, according to NDATUS. Total expenditures for drug treatment in real terms (i.e., inflation adjusted) between 1976 and 1987 declined by 15 percent. Funding per patient, in real dollars declined 25 percent for outpatient, 30 percent for methadone maintenance, and 15 percent for residential treatment during this period. Government (State, Federal, and local) financed 90 percent of the treatment revenues reported in 1976; by 1987, the government share declined to 55 percent. Private financing (i.e., insurance and private pay) now covers 40 percent of total drug abuse treatment costs, with the majority (75 percent) of these payments going to hospitals. Average public sector expenditure per treated client is down 40 percent in real terms from 1976 to 1987.

Accomplishments

Among the services research accomplishments for FY 1989 are the following:

Quantification of Drug Treatment Utilization and Costs Under Medicare: Targeted research has been undertaken to describe changes in the number of inpatient hospital discharges associated with treatment for alcohol and other drug use in the Medicare inpatient program. Medicare-covered inpatient treatment for drug abuse increased by 86 percent from FY 1984-1987, with the number of discharges increasing from 7,300 to more than 13,700. During this period, treatment for alcohol abuse remained almost flat, rising little more than 1 percent annually. It is noteworthy that during the 1984-87 period, total discharges for Medicare inpatient services decreased 10.6 percent. This means that direct drug abuse treatment utilization and cost, while small in absolute terms, today represents an increasing share of overall Medicare inpatient services.

Quantifying the Medical Cost Consequences of Drug Abuse, Alcohol Abuse, and Mental Illness: Recent studies in both inpatient (hospital) and ambulatory or residential (non-hospital) settings clearly document an increase in the number of clients seeking detoxification and rehabilitation services. For the most part, these studies have addressed only the treatment of the substance abuse problems, and do not include the utilization or costs of health services consumed to treat the consequence of drug abuse (e.g., drug poisoning).

In order to measure more precisely total inpatient health care utilization and costs attributable to the substance abusing population, a paradigm has been developed to classify diagnoses according to a scale of relatedness to substance abuse problems. By examining all diagnostic classifications rather than focusing exclusively on diagnoses which are principally responsible for a given episode of care, all identifiable substance abuse-related comorbid conditions can be included in these estimates.

The paradigm has been used to develop estimates for Medicare beneficiaries. Analysis of Medicare inpatient hospital claims records demonstrates that ADM related morbidity is present in substantially more hospitalized persons than has traditionally been recognized. Using traditional estimates of direct ADM treatment expenditures and utilization, approximately 3.2 percent of Medicare total inpatient costs and admissions in 1987 were to treat ADM disorders. Using the co-morbidity paradigm, upwards of 11 percent of the Medicare patients were found to have at least one definite ADM-related diagnosis. These patients had a 25 percent greater admission rate and were hospitalized 30 percent longer than the average Medicare patient with a hospital admission. Inpatient hospital costs for these patients averaged 16 percent greater than the average cost for all other Medicare patients with at least one hospitalization.

INDIAN HEALTH SERVICE

Alcoholism and Substance Abuse Services

Since 1978, the alcoholism age adjusted death rate among American Indians/Alaska Natives (AI/AN) has declined by approximately 52 percent. This improvement can be attributed to several factors:

- the continued training of Indian Health Service (IHS) and Bureau of Indian Affairs (BIA) staff, community members, and IHS Primary Care Providers;
- the increased number of alcoholism and substance abuse programs from 36 to over 309; and, most importantly AI/AN communities are taking responsibility for their own wellness;
- a continued emphasis on the concepts of wellness, health promotion/disease prevention.

Revision of the Chemical Dependency Management Information System will be completed in Fiscal Year (FY) 1990. Implementation of the system on a service-wide basis will begin in FY 1990 to better manage all inpatient, outpatient, education and prevention activities.

Anti-Drug Abuse Activities (Public Law 99-570 and Public Law 100-690)

Five Youth Regioanl Treatment Centers (RTCs) authorized by Public Law (P.L.) 99-570 are operational. These include Alaska, Albuquerque, Oklahoma City, Nashville, and Navajo IHS Areas. Three other IHS Areas (Phoenix, Aberdeen, and Portland) are renovating facilities and are expectd to be operational in FY 1991-1992. The remaining Areas are providing inpatient chemical dependency treatment through contracts pending completion of their plans for RTCs. Plans are currently being developed for each Area to assure access to inpatient treatment by youth. Resources from the existing IHS alcoholism program (P.L. 94-437) augment the adolescent alcoholism and substance abuse program by providing for a broader range of comprehensive services.

Expanded community education and training activities will continue to be provided for Indian leaders, community members, BIA and IHS staff. More than 1,000 health care providers have been targeted to receive training in alcohol and other drug abuse prevention and treatment this year.

Alcohol continues to be the drug of choice in Indian Country. However, alcohol and poly-drug use, specifically cannabis, cocaine, and opiates, are increasing among AI/AN adults and adolescents. With the passing of P.L. 99-570 and P.L. 100-690, increased chemical dependency treatment, education, and prevention activities are provided to meet this need.

In FY 1990, adult and youth community rehabilitation, aftercare, and follow-up services will continue to be developed and will enhance the basic alcoholism and substance abuse program.

The IHS will continue to work with the AI/AN communities to integrate the treatment and prevention of alcoholism and substance abuse into the health delivery system.

CENTERS FOR DISEASE CONTROL

SUBSTANCE ABUSE

HIV prevention among drug abusers is accomplished in several ways through programs funded by CDC. For example, community activities are often conducted by former addicts providing education, referral to drug treatment, and other risk reduction messages to IVDUs and their sex partners. These activities also include street outreach programs. Support for these activities is provided by the HIV prevention and surveillance cooperative agreements and the direct funding of minority and other community-based organizations.

CDC has developed a model joint plan for use by State/local health departments and State drug agencies to assist them in providing comprehensive HIV/STD/TB prevention programs in drug treatment centers.

In 1991 an increase of $4,975,000 will be used to assess the effectiveness of street outreach in reducing high-risk behaviors associated with HIV infection in IVDUs and their sex partners. HIV counseling and testing services will continue to be provided to IVDUs and their sexual partners in drug treatment centers, public health clinics, (i.e., STD, women's health, and TB clinics), and alternate test sites.

FOOD AND DRUG ADMINISTRATION
SUBSTANCE ABUSE PROGRAM

As part of its regulatory responsibilities, FDA has maintained an ongoing program of monitoring methadone narcotic treatment centers to assure their compliance with established standards related to DEA registration. In keeping with the national drive to address the continuing problem of drug abuse, FDA is expanding this monitoring program as well as continuing its pursuit of the abusive use of approved drugs such as steroids and non-approved look alike drugs (substances designed to look like drugs of abuse, which tend to glamorize them, and which often contain illegal drugs or illegal combinations of substances).

The FDA methadone monitoring program is concentrating on a positive approach, conducting site visits to a potentially expanding number of methadone treatment centers to identify specific areas where assistance can be provided to improve operations and assure compliance. Areas targeted include

- the availability and provision of appropriate counseling and support services;
- the conduct of proper screening procedures to prevent the provision of treatment services to non-addictive persons and pregnant women;
- the development and administration of proper dose regimens under medical supervision required for satisfactory detoxification; and
- the conduct of appropriate client interviews by medical personnel to assess degree of addiction and document personal history.

In addition, the agency is expanding the training of field investigative staff to broaden their knowledge base regarding regulations and enforcement policy and procedures.

FDA remains very concerned about the evidence of widespread illegal use of look-alike and approved drugs, especially steroids. Distribution channels and activities closely resemble those for other illicit drugs such as cocaine. Under the newly-enacted Drug Abuse legislation, penalties for distribution have been increased in severity and FDA's activities in this regard are being strengthened in an effort to curb this abuse. Comprehensive investigation into the illegal use of steroids is being expanded and public education and outreach efforts targeted at users has been increased as a critical method for reducing this abuse.

Also, FDA continues its role of reviewing applications for drugs for the treatment of drug abuse. FDA also plays a consultative role with DEA on issues related to the scheduling of controlled substances, and advises on the legitimate uses and levels of supply needed for controlled substances which have approved medical uses.

OFFICE OF HUMAN DEVELOPMENT SERVICES

Substance Abuse

- The Drug Education and Prevention Relating to Youth Gangs Program authorizes grants to or contracts with public and non-profit private agencies, organizations, institutions and individuals and requires coordination with juvenile justice programs to ensure that activities are complementary, not duplicative. Funds are intended to prevent and reduce illicit drug related activities by youth gang members; educate youth about such abuse; support local police educational outreach activities; inform gang members and their families about drug abuse treatment services; and provide technical assistance.

  During fiscal year 1989, $15 million was awarded to support community-based consortia in 22 States, the District of Columbia and Puerto Rico; to demonstrate innovative support programs for youth and their families; and to carry out specific prevention, diversion, and intervention activities with at-risk youth.

  In fiscal years 1990 and 1991, $14,801,000 will be used to support the continuation of discretionary demonstrations in the areas of community-based prevention, diversion, family support, and public education activities. Efforts to improve school and community operation and coordination of youth service systems will also be continued, as well as contracts in the areas of technical assistance for grantees and communities and monitoring and evaluation of grant projects.

- The Drug Education and Prevention Program for Runaway and Homeless Youth authorizes grants to public and private non-profit agencies, organizations and institutions for research, demonstration and service projects, but requires the Secretary to give priority to agencies that have experience in providing services to runaway and homeless youth. Grants under this program support counseling, community education, training and information, research, and other activities to improve the availability and coordination of local services related to drug abuse for runaway and homeless youth.

During fiscal year 1989, competitive grant awards were made to 104 agencies and organizations representing 35 States and the District of Columbia to improve or expand existing services; develop networking efforts in rural and other areas with minimal services; develop innovative model programs; and serve Native American youth. In addition, a contract was awarded to develop a prototype drug education training program and to provide technical assistance to runaway and homeless youth service providers.

In fiscal years 1990 and 1991, $14,801,000 will support the continuation of service and demonstration grants related to drug abuse in the areas of comprehensive service delivery and resource development for runaway and homeless youth and their families and for training programs for youth service providers and of contracts for research, technical assistance, monitoring and evaluation of grantee activities.

- States may use Social Services Block Grant (SSBG) funds for substance abuse activities. In fiscal year 1988, 10 States used part of their SSBG funds for this purpose. Because States are not required to report to the Federal government the dollar amounts for services provided through the SSBG, it is not possible to report the level of funding allotted to substance abuse activities under the SSBG.

- The Abandoned Infants Assistance Act of 1988 (P.L. 100-505), first funded in FY 1990, will fund demonstration projects regarding the non-medical care of infants and young children abandoned by drug-using parents, including HIV-positive children.

- In addition to programs mandated specifically for the prevention of substance abuse, HDS has used its discretionary program authorities to support additional projects focused on drug abuse and/or alcoholism. For instance in FY 1987, HDS awarded four three-year demonstration grants, authorized by the Child Abuse Prevention and Treatment Act, designed to reduce the risk of abuse and neglect in infants born to chemically-dependent mothers by demonstrating effective methods for providing services and training. Training materials, model curricula and replicable program models resulting from these projects will be used to implement strategies for interagency coordination and to provide specialized training for service providers working with chemically dependent mothers and

their children. In FY 1989, a two-year research project to conduct a "National Study of Maltreatment of Handicapped Children and Child Maltreatment in Substance Abusing Families" was funded to estimate the current national extent of child abuse and neglect among these populations and to examine how decision-making processes affect the services provided for these children and families.

Another example is the use of funds from the Native American Programs Act and the Child Welfare Services Research and Demonstration Program under Section 426 of the Social Security Act in FY 1988 to support five two-year projects focused on treatment services for American Indian families with children in foster care or at-risk of placement due to parental alcoholism or substance abuse. An evaluation study, funded in FY 1989, will provide information on effective program implementation procedures that can be replicated with other Indian Tribes.

In fiscal year 1991, an additional $6 million has been requested under section 426 of the Social Security Act. The additional funds will be used for one-time demonstration projects to increase access to comprehensive multidisciplinary serivces to meet the immediate nonmedical needs of infants born of crack-cocaine using mothers and infants born HIV-positive.

Department of Health and Human Services
National Support for Performance of Medical and Health-Related R&D,
by Source of Funds, 1968-1989*

H-1

(Millions of Dollars)

Source of Funds	1968	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978
Total	$2,568	$2,785	$2,847	$3,168	$3,536	$3,750	$4,443	$4,701	$5,107	$5,568	$6,262
Government	1,699	1,818	1,837	2,075	2,375	2,470	3,008	3,118	3,371	3,734	4,227
Federal	1,582	1,674	1,667	1,877	2,147	2,225	2,754	2,832	3,059	3,396	3,811
NIH	(864)	(893)	(873)	(1,039)	(1,271)	(1,323)	(1,737)	(1,880)	(2,060)	(2,280)	(2,581)
State & local	117	144	170	198	228	245	254	286	312	338	416
Industry	661	754	795	860	934	1,048	1,183	1,319	1,469	1,614	1,800
Private nonprofit	208	213	215	233	227	232	252	264	267	220	236
Foundations	72	69	69	83	77	75	79	86	76	71	65
Voluntary health agencies	57	61	61	63	63	70	84	85	94	102	113
Howard Hughes Medical Institute	0	0	0	0	0	0	0	0	0	0	0
Other	79	83	85	87	87	87	89	93	97	47	57

*Excludes research training and construction. Includes U.S.-funded health R&D support spent abroad. Revised data for 1970 forward. Estimates for 1977 forward are of private educational institutions' own funds only. Data are no longer available on which to base estimates of private endowments' and individuals' contributions to health R&D.

Note: Federal data are obtained via an interagency survey conducted by the National Institutes of Health. Estimates for State and local governments include awards made by governmental agencies, as well as appropriations made to educational institutions for the performance of health R&D. The industry sector includes data for the pharmaceutical, medical supply, biomedical engineering, and biotechnology industries. The non-industrial private sector covers the funds provided by philanthropic foundations, voluntary health agencies, the Howard Hughes Medical Institute, and other private contributors for the support of health R&D.

Department of Health and Human Services
National Support for Performance of Medical and Health-Related R&D,
by Source of Funds, 1968-1989*

(Millions of Dollars)

Source of Funds	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988 (est.)	1989 (proj.)
Total	$7,133	$7,935	$8,703	$9,483	$10,634	$12,014	$13,408	$14,801	$16,827	$18,729	$20,575
Government	4,786	5,203	5,413	5,605	6,112	6,880	7,665	7,922	8,973	9,726	10,547
Federal	4,321	4,723	4,848	4,970	5,399	6,087	6,791	6,895	7,827	8,454	9,207
NIH	(2,953)	(3,182)	(3,333)	(3,433)	(3,789)	(4,257)	(4,828)	(5,005)	(5,851)	(6,291)	(6,792)
State & local	465	480	564	634	712	793	874	1,026	1,146	1,272	1,339
Industry	2,093	2,459	2,998	3,561	4,145	4,643	5,244	6,166	7,130	8,260	9,259
Private nonprofit	254	274	292	318	377	491	500	714	725	744	770
Foundations	60	54	52	44	82	113	89	83	115	97	82
Voluntary health agencies	129	146	161	178	188	187	213	238	257	287	310
Howard Hughes Medical Institute	0	0	0	0	0	79	65	247	183	179	188
Other^	66	73	79	96	107	112	133	146	170	181	191

*Excludes research training and construction. Includes U.S.-funded health R&D support spent abroad. Revised data for 1970 forward. ^Estimates for 1977 forward are of private educational institutions' own funds only. Data are no longer available on which to base estimates of private endowments' and individuals' contributions to health R&D.

Note: Federal data are obtained via an interagency survey conducted by the National Institutes of Health. Estimates for State and local governments include awards made by governmental agencies, as well as appropriations made to educational institutions for the performance of health R&D. The industry sector includes data for the pharmaceutical, medical supply, biomedical engineering, and biotechnology industries. The non-industrial private sector covers the funds provided by philanthropic foundations, voluntary health agencies, the Howard Hughes Medical Institute, and other private contributors for the support of health R&D.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

H-4

National Institutes of Health

History of Congressional Action on Budget Requests 1/
for National Institutes of Health Institutes and Research Divisions

	Budget Estimate to Congress	Appropriation
1933	$48,000	$48,000
1934	54,775	54,775
1935	50,000	50,000
1936	64,000	64,000
1937	64,000	64,000
1938	464,000	464,000
1939	515,000	515,000
1940	587,750	707,000
1941	712,120	711,000
1942	705,000	700,000
1943	1,278,270	1,278,270
1944	2,291,000	2,555,020
1945	2,835,000	2,835,000
1946	3,078,000	3,414,700
1947	10,799,500	8,125,448 2/
1948	22,403,000	28,876,000
1949	45,701,460	37,668,000
1950	40,567,000	50,167,000
1951	49,845,000	47,334,750 2/
1952	53,386,000	52,447,781
1953	55,005,000	59,030,750
1954	56,240,000	71,153,000
1955	71,128,000 4/	81,268,000
1956	90,023,000 5/ 6/	98,450,000
1957	126,725,000 7/	183,007,000
1958	190,183,000	211,183,000
1959	211,814,000	294,383,000
1960	294,279,000	400,000,000
1961	400,000,000	560,000,000 8/
1962	582,000,000	738,335,000 9/
1963	780,400,000	880,830,000
1964	930,454,000	918,454,000
1965	956,492,000	965,992,000
1966	1,105,006,000 10/	1,138,406,000
1967	1,231,764,000	1,306,983,000
1968	1,152,250,000 11/	1,143,424,000
1969	1,188,293,000	1,100,092,000
1970	1,064,870,000 12/	1,122,718,400 13/
1971	1,099,249,000	1,196,249,000
1972	1,333,916,000 14/	1,476,046,000
1973	1,483,982,000 15/	1,713,455,000
1974	1,531,776,000	1,744,554,000 16/
1975	$1,785,922,000	$2,043,721,000
1976	2,349,413,000 17/	2,627,845,000
1977	2,088,179,000	2,424,519,000
1978	2,456,104,000	2,720,767,000 18/
1979	2,794,623,000	3,097,138,000 19/
1980	3,111,391,000	3,360,670,000
1981	3,432,146,000	3,490,459,000 20/
1982	3,239,274,000 21/	3,563,324,000 22/
1983	3,660,945,000	3,929,843,000 22/
1984	3,980,856,000	4,374,768,000 23/
1985	4,476,524,000	5,033,515,000
1986	4,748,750,000	5,308,754,000 24/
1987	4,936,157,000	6,031,964,000 25/
1988	5,407,785,000 26/	6,666,693,000
1989	6,407,168,000	7,245,836,000 27/
1990	6,776,727,000 28/	7,443,452,000 29/
1991	7,668,495,000	

NOTE: Not all amounts on this table are comparable from year to year because of changes in the content of the appropriations.

1/ This table excludes the National Library of Medicine, Office of the Director, and Buildings and Facilities. H4[illegible]3

2/ Includes $386,500 in transfers.

3/ Not less than $3,000,000 was earmarked for liquidating cash; an additional $1,175,000 was used for that purpose.

4/ Excludes $3,216,250 rescinded.

5/ Excludes $131,000 for Gorgas Memorial Laboratory.

6/ Excludes $147,000 for Gorgas Memorial Laboratory.

7/ Includes $90,500 transfer.

8/ Includes $200,000 transfer from other appropriations.

9/ Includes $12,129,000 for construction of mental health-neurology research facility.

10/ Includes $1,000,000 for planning for a gerontological research facility,and $750,000 for modernization at the Rocky Mountain Laboratory, Hamilton, Montana.

11/ Includes $25,000,000 for Regional Medical Programs, $19,700,000 for Mental Health Staffing, and $20,250,000 for Heart Disease, Cancer and Stroke Program.

12/ Includes $246,741,000 for National Institute of Mental Health Includes $20,616,000 for Environmental Health Sciences. $20,616,000 for Environmental Health Sciences.

13/ Excludes $7,093,000 for the Office of the Director, NIH.

14/ Includes $1,348,200 supplemental.

15/ Includes $142,075,000 in supplementals.

16/ Excludes DBS. Request reflects amendment.

17/ House allowance reflects maximum authorized. Reflects P.L. 93-192.(?)

18/ Request reflects amendment requested for 1976 in 1977 budget submission. Estimate and appropriation includes the Transition Quarter 15 month period.

19/ Continuing Resolution was Conferees Allowance. Includes supplemental of $17,834,000.

20/ Includes Continuing Resolution for items not considered in P.L. 95-482.

21/ Reflects a rescission of $46,959,000 authorized under P.L. 97-12

22/ Reflects the September amendment. the original request was $3,680,994,000.

23/ Continuing Resolution.

24/ Includes Continuing Resolution for items not considered in P.L. 98-139.

25/ Reflects transfer of $4,500,000 to DHHS from NCI for the Mary Babb Randolph Cancer Center and an administrative reduction of $3,000,000.

26/ Includes supplemental of $2,250,000.

27/ Does not include administrative reduction of $86,947,000 or procurement reduction of $6,684,000.

28/ Excludes $752,670,000 for AIDS research proposed for consolidation in OASH.

29/ Includes $752,670,000 for AIDS research.

H-4

ALCOHOL DRUG ABUSE AND MENTAL HEALTH ADMINISTRATION

History of Congressional Action of Budget Requests

Year	Budget Estimate to Congress	Appropriation
1947	$4,478,000	-0-
1948	5,108,000	$4,250,000
1949	11,501,000	9,128,000
1950	9,662,000	10,862,000
1951	7,569,000	7,130,000 1/
1952	10,022,000	9,988,773
1953	10,917,000	10,895,000
1954	9,817,000	12,095,000
1955	12,640,000	14,147,000
1956	17,751,000	18,001,000
1957	21,749,000	35,197,000
1958	35,217,000	39,217,000
1959	37,788,000	52,419,000
1960	52,384,000	68,090,000
1961	67,563,000	100,900,000
1962	88,324,000	108,876,000
1963	126,899,000	143,599,000
1964	190,096,000	183,288,000
1965	224,085,000	222,932,000
1966	278,669,000	282,669,000
1967	305,115,000	315,619,000
1968	346,909,000	346,909,000
1969	364,939,000	350,439,000
1970	357,904,000	360,302,000
1971	346,656,000	389,238,000
1972	500,263,000	613,013,000
1973	603,719,000	803,823,000
1974	645,533,000 2/	815,975,000 3/
1975	692,190,000	795,636,000
1976	653,627,000	813,402,000
T.Q.	129,855,000	117,363,000
1977	645,509,000	885,571,000
1978	881,293,000	941,668,000
1979	1,002,871,000	1,025,085,000
1980	1,115,768,000	1,111,146,000
1981	1,092,724,000	1,024,734,000
1982	821,823,000	860,178,000
1983	372,682,000	885,849,000
1984	420,570,000	915,759,000

ALCOHOL DRUG ABUSE AND MENTAL HEALTH ADMINISTRATION

History of Congressional Action of Budget Requests

Year	Budget Estimate to Congress	Appropriation
1985	421,250,000	923,626,000 4/
1986	886,194,000	968,860,000
1986 Sequester	---	-41,661,000
1987	892,240,000	1,062,365,000
1987 Supplmntl	231,000,000 5/	312,700,000 5/
1987 Reappropr	(5,000,000)	---
1988	1,042,873,000	1,373,727,000
1989	1,504,413,000	1,562,712,000
1989 Supplmntl	---	283,000,000
1990	1,738,716,000	1,926,818,000 6/
1990 Sec 518 Red.	---	-1,135,000
1990 (DOT Appr)	300,000,000	727,000,000
1990 Sequester	---	-26,745,000
1991	2,831,511,000 7/	

1/ Excludes $495,000 rescinded.

2/ Excludes $636,180,000 for outyear costs not considered by Congress.

3/ Includes $23,114,000 withheld in accordance with P.L. 93-192.

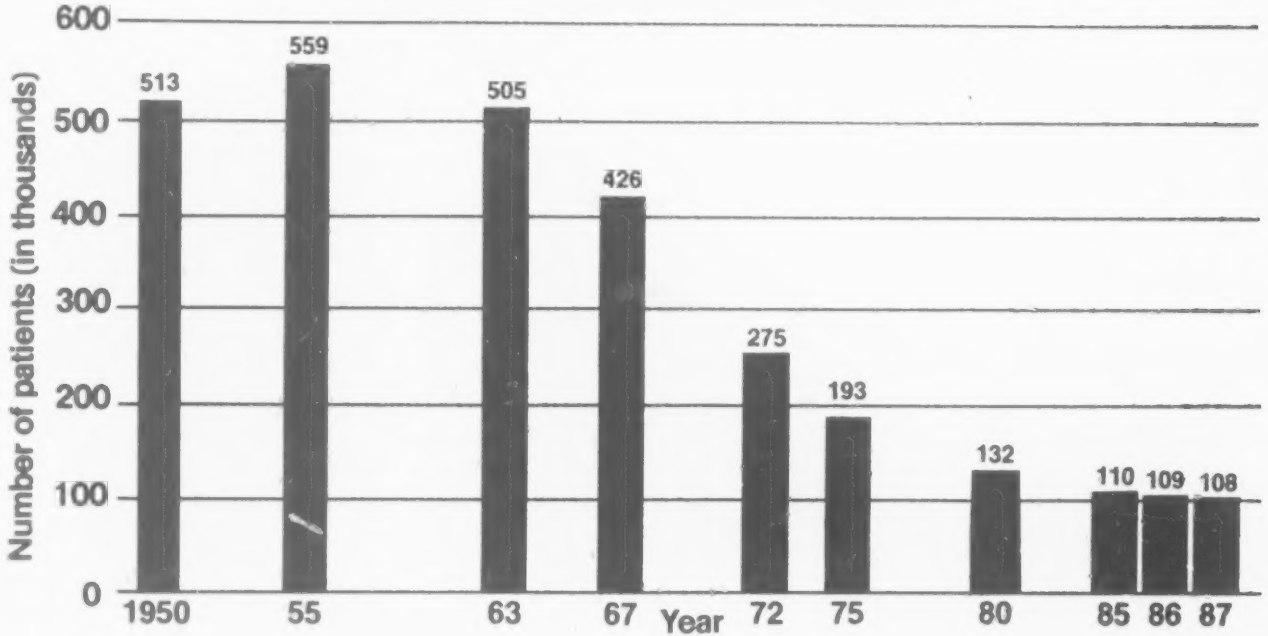
4/ Excludes $1,495,000 withheld in accordance with Section 515 of the Treasury-Postal Service Appropriation Act, 1985.

5/ Includes $50,700,000 for the Homeless Act.

6/ Excludes $7,359,000 in FY 1991 Advance Funding for Homeless.

7/ Includes $7,359,000 in FY 1991 Advance Funding for Homeless.

Actual number of resident patients, end of year, State and county mental hospitals, selected years 1950-1987



DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE

Funds Available for Obligation for More than One Year

Appropriation	Program	Length of Availability	Authority
Health Resources and Services.....	Medical Facilities Guarantee and Loan Fund	Until expended	Titles XVI of the PHS Act Section 1602
Health Resources and Services.....	Health Teaching Facilities Interest Subsidies	Until expended	Title VII, Section 720 of the PHS Act
Health Resources and Services.....	Health Professions Graduate Student Loan Insurance Fund	Until expended	Title VII, Section 727 of the PHS Act
Health Resources and Services.....	Health Professions Student Loan Revolving Fund	2 Year	Title VII, Section 741 of the PHS Act
Health Resources and Services.....	Nursing Student Loan Revolving Fund	2 Year	Title VII, Section 838 of the PHS Act
Health Resources and Services.....	Vaccine Improvement Program Trust Fund	Until expended	PHS Act XXI, Subtitle 2

DEPARTMENT OF HEALTH AND HUMAN SERVICES

CENTERS FOR DISEASE CONTROL

Funds Available for Obligation for More than One Year

Appropriation	Program	Length of Availability	Authority
Disease Control, Research, and Training:	Buildings & Facilities	Indefinite	Appropriation Language & Public Health Service Act Section (321(a))
	Health Statistics (Reimbursements only)	Indefinite	Economy Act (31 USC 1535) and Appropriation Language

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Funds Available for Obligation for More Than One Year

Appropriation	Program	Length of Availability	Authority
Buildings and Facilities	Direct construction	Until expended	Public Health Service Act Title IV, Section 402b (4A)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Alcohol, Drug Abuse, and Mental Health Administration

Funds Available for Obligation for More than One Year

Appropriation	Program	Length of Availability	Authority
St. Elizabeth's Hospital	Construction and Renovation	Indefinite	P.L. 98-621
ADAMHA	Royalties	FY 1991	P.L. 99-502
ADAMHA	Buildings and Facilities	Indefinite	P.L. 99-660

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service

Indian Health Service

Funds Available for Obligation for More Than One Year

Appropriation	Program	Length of Availability	Authority
Indian Health Facilities . . .	Hospitals	Until Expended	25 USC 13, Snyder Act, and P.L. 83-568, Transfer Act, 42 USC 2001.
	Outpatient Care Facilities	Until Expended	25 USC 13, Snyder Act, and P.L. 83-568, Transfer Act, 42 USC 2001.
	Sanitation Facilities	Until Expended	P.L. 86-121, Indian Sanitation Facilities Act; Title III of P.L. 94-937, Indian Health Care Improvement Act; and P.L. 96-537, Indian Health Care Amendments of 1980, and P.L. 100-713 of 1988.
	Personnel Quarters	Until Expended	25 USC 13, Snyder Act, and P.L. 83-568, Transfer Act, 42 USC 2001.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service

Indian Health Service

Funds Available for Obligation for More Than One Year

Appropriation	Program	Length of Availability	Authority
Indian Health Services	Medicare/Medicaid - Reimbursements into fund established by Sections 401 402 of Indian Health Care Improvement Act.	3 Years	Section 401 and 402 of the Indian Health Care Improvement Act, P.L. 94-437, and annual Appropriations Act.
	Permanent appropriation established by Section 320, P.L. 98-473, 1985, continuing appropriations for maintenance and operations of IHS Personnel Quarters.	Until Expended	Section 320, P.L. 94-473.
	Indian Catastrophic Health Emergency Fund and Contract Health Care	Until Expended	P.L. 99-500 and P.L. 99-591, FY 1987 Continuing Appropriations Act, Sec. 101(h) P.L. 100-446 for P.L. 101-100-P.L. 101-121
	Indian Health Scholarship Program (Section 103 of the Indian Health Improvement Act and Section 338G of the Public Health Service Act).	2 Years	P.L. 99-500 and P.L. 99-591. P.L. 101-100 P.L. 101-121 P.L. 101-164

27-519 O—90—38

DEPARTMENT OF HEALTH AND HUMAN SERVICES
SOCIAL SECURITY ADMINISTRATION
Funds Available for Obligation for More Than One Year

Appropriation	Program	Length of Availability	Authority
Limitation on Administrative Expenses (Construction)	The construction activity provides funds for the construction needs of the Social Security programs. Beginning in 1985, construction funds are no longer being requested as a no-year appropriation. Unobligated balance at the end of FY 1989--$7,505,018.	Until expended	Section 201(g) of the Social Security Act and P.L. 98-139.
Limitation on Administrative Expenses (Automatic data processing and telecommunications activities)	Congress had earmarked extended availability of funds for automatic data processing and telecommunication leases, purchases or contracts for the purpose of systems modernization and major telephone systems acquisitions. That authority ended with the passage of P.L. 100-436. Funds available under prior authority in 1990--unobligated balance from prior years: $3,178,000; expected recoveries from prior year obligations: $5,000,000.	Until expended	Section 201(g)(1) of the Social Security Act and P.L. 100-202.

T-1

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Human Development Services

(Name of OPDIV)

Funds Available for Obligation for More than One Year

Appropriation	Program	Length of Availability	Authority
75X1634	Grants to States for Social and Child Welfare Services	Indefinite	Section 20, 2002, and 2002 of the Social Security Act

DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE

Requests in the FY 1991 Budget for Which Legislative

Authority has Expired or is Due to Expire on September 30, 1990

(Dollars in thousands)

Appropriation/ Program	Expiring Authorization	Amounts Included in President's Budget
NHSC Field	Sec. 338 (a)	42,361
State Loan Repayment	Sec. 338 (H)	---

T-2

DEPARTMENT OF HEALTH AND HUMAN SERVICES

CENTERS FOR DISEASE CONTROL

Requests in the FY 1991 Budget for Which Legislative Authority has Expired or is Due to Expire on September 30, 1990

(Dollars in thousands)

Appropriation/Program	Expiring Authorization	Amounts Included in President's Budget
Immunization Grants	Public Health Service Act (PHSA) Section 317 (J)(1)(A)	$130,862 1/
Tuberculosis Grants	PHSA Section 317(J)(2)	8,334 1/
Injury Control	PHSA Section 394(a)	22,660 1/

1/ Authorization expires September 30, 1990. An extension is pending.

T-2

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Alcohol, Drug Abuse, and Mental Health Administration

Requests in the FY 1991 Budget for Which Legislative
Authority has Expired or is Due to Expire on September 30, 1990

(Dollars in thousands)

Appropriation/Program	Expiring Authorization	Amounts Included in President's Budget
Grant Program for Demo Projects Community Support Programs	520 PHS	$26,862

DEPARTMENT OF HEALTH AND HUMAN SERVICES T-2

PUBLIC HEALTH SERVICE

ASSISTANT SECRETARY FOR HEALTH

Requests in the FY 1991 Budget for Which Legislative Authority has Expired or is Due to Expire on September 30, 1990

(Dollars in thousands)

Appropriation/ Program	Expired Authorization	Amounts Included in President's Budget
Office of the Assistant Secretary for Health:		
Adolescent Family Life	PHSA Title XX	$9,431
Family Planning	PHSA Title X	139,135

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Family Support Administration
Office of Refugee Resettlement

Requests in the FY 1991 Budget for Which Legislative Authority has Expired or is Due to Expire on September 30, 1990

(Dollars in Thousands)

Appropriation Program	Expiring Authorization	Amounts included in President's Budget
75-1503-0-1-609		
Refugee and Entrant Assistance	The Refugee Assistance Extension Act of 1986 (P.L. 99-605)	$ 368,822
75-1502-0-1-609		
LIHEAP	The Omnibus Budget Reconciliation Act of 1981	$1,050,000

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of Human Development Services
(Name of OPDIV)

Requests in the FY 1991 Budget for Which Legislative Authority has Expired or is Due to Expire on September 30, 1990

(Dollars in thousands)

Appropriation/Program	Expiring Authorization	Amounts Included in President's Budget
Head Start	Section 39 of the Head Start Act, as amended	$1,886,315,000
Child Development Associate Scholarships	Section 606 of the Child Development Associate Scholarships Assistance Act of 1985	1,431,000
Dependent Care Planning and Development	Section 607(A) of the State Dependent Care Development Grants Act	13,178,000
Developmental Disabilities State Grants	Section 130 of the Developmental Disabilities Assistance and Bill of Rights Act, as amended	61,939,000
Developmental Disabilities Protection and Advocacy	Section 143 of the Developmental Disabilities Assistance and Bill of Rights Act, as amended	20,484,000
Developmental Disabilities Projects of National Significance	Section 163 of the Developmental Disabilities Assistance and Bill of Rights Act, as amended	2,862,000

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of Human Development Services
(Name of OPDIV)

Requests in the FY 1991 Budget for Which Legislative Authority has Expired or is Due to Expire on September 30, 1990

(Dollars in thousands)

Appropriation/Program	Expiring Authorization	Amounts Included in President's Budget
Developmental Disabilities University Affiliated Facilities	Section 164 of the Developmental Disabilities Assistance and Bill of Rights Act, as amended	13,192,000

DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUMMARY

Budgeted Full-Time Permanent Employment, Fiscal Years 1990 and 1991

	FY 1990				FY 1991		
Appropriation	Authorized Positions	Estimated FTE	On Duty 12/31/89	Anticipated On Duty 09/30/90	Positions Requested	Estimated FTE	Anticipated On Duty 09/30/91
PUBLIC HEALTH SERVICE							
Health Resources and Services Administration	2,243	2,216	2,094	2,036	2,072	1,956	1,843
Centers for Disease Control	5,320	5,027	4,548	5,320	5,417	5,132	5,417
National Institutes of Health	11,470	13,779	10,973	11,470	11,470	14,133	11,470
Alcohol, Drug Abuse, and Mental Health	1,504	1,912	1,423	1,530	1,611	2,048	1,638
Health Care Policy and Research	144	167	104	141	153	178	150
Office of the Assistant Secretary for Health	699	743	732	745	759	819	744
Subtotal, PHS (Labor/HHS)	21,380	23,844	19,874	21,242	21,482	24,266	21,262
Food and Drug Administration	7,685	7,877	7,183	7,329	8,366	8,444	7,749
Indian Health Service	12,409	12,586	10,904	10,965	12,489	12,751	11,109
Total, PHS	41,474	44,307	37,961	39,536	42,337	45,461	40,120

DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUMMARY

Budgeted Full-Time Permanent Employment, Fiscal Years 1990 and 1991

	FY 1990				FY 1991		
Appropriation	Authorized Positions	Estimated FTE	On Duty 12/31/89	Anticipated On Duty 09/30/90	Positions Requested	Estimated FTE	Anticipated On Duty 09/30/91
HEALTH CARE FINANCING ADMINISTRATION	4,314	4,017	4,019	4,017	4,424	4,127	4,127
SOCIAL SECURITY ADMINISTRATION	66,000	59,926	60,330	61,134	66,000	60,364	61,000
FAMILY SUPPORT ADMINISTRATION	1,069	1,029	993	1,013	1,029	1,029	1,017
OFFICE OF HUMAN DEVELOPMENT SERVICES	978	975	947	971	975	975	975
OFFICE OF THE SECRETARY	4,535	4,415	3,914	4,483	4,509	4,389	4,475
Office of Consumer Affairs	22	22	23	21	22	22	21
Subtotal, HHS (Labor/HHS)	98,276	94,206	90,077	92,860	98,419	95,150	92,856
TOTAL, HHS	118,392	114,691	108,187	111,175	119,296	116,367	111,735

DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUMMARY

Fiscal Years 1971 through 1991 Total Employment: Authorized Positions, End-of-Year Employment, and Full-Time Equivalents (FTE)

	1971	1972	1973	1974	1975	1976	1977
Total authorized positions	97,456	97,770	110,420	122,336	126,349	130,934	135,881
Total, end-of-year employment	95,579	97,517	107,105	116,950	120,849	128,993	131,544
Total, FTE employment *	100,698	100,590	125,630	135,231	140,588	143,869	147,388

	1978	1979	1980	1981	1982	1983	1984
Total authorized positions	138,148	147,515	144,663	146,037	136,651	135,586	135,946
Total, end-of-year employment	134,219	138,647	136,483	139,972	133,201	134,347	131,894
Total, FTE employment *	148,684	158,250	157,000	148,858	142,520	141,757	136,946

	1985	1986	1987	1988	1989	1990	1991
Total authorized positions	129,506	125,909	120,823	119,613	118,060	118,002	118,835
Total, end-of-year employment	125,762	120,644	116,360	116,378	115,701	117,242	118,166
Total, FTE employment *	132,274	127,183	121,862	119,100	118,035	116,999	118,442

* Work years shown prior to FY 1981.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUMMARY

Entertainment Fund Authorization for Fiscal Year 1990
and Amount Expended

Appropriation	Authorized for FY 1990	Expended in FY 1990	FY 1991 Budget Request
PUBLIC HEALTH SERVICE			
Office of the Assistant Secretary for Health	$9,500	$9,500	$9,500
HEALTH CARE FINANCING ADMINISTRATION	2,000	500	2,000
OFFICE OF THE SECRETARY	15,000	4,800	15,000
TOTAL, HHS	$26,500	$14,800	$26,500

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUMMARY

New Programs in 1991 Budget
(Dollars in thousands)

Appropriation/Program	1991 Budget Request
PUBLIC HEALTH SERVICE:	
Health Resources and Services Admin:	
-- Health Services in Underserved Neighborhoods	$35,000
-- Health Professions Institutional Assistance - Faculty Development	12,000
-- Community Based Recruitment and Support	5,000
Centers for Disease Control	11,500
Office of the Assistant Secretary for Health	139,135
Subtotal, PHS (Labor/HHS)	202,635
Indian Health Service:	
-- Tribal Health Administration	22,600
-- Federal Indian Health Administration	877,625
-- Indian Health Facilities	3,000
Total, PHS	1,105,860
HEALTH CARE FINANCING ADMINISTRATION	510,000
FAMILY SUPPORT ADMINISTRATION:	
Fiscal Assistance for Puerto Rico	825,000
TOTAL, HHS	$2,440,860

DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUMMARY

ANALYSIS OF UNOBLIGATED CARRYOVER BALANCES

Fiscal Years 1989, 1990 and 1991
(Dollars in thousands)

Appropriation	Balance end of FY 1989	Balance end of FY 1990	Balance end of FY 1991
PUBLIC HEALTH SERVICE			
Health Resources and Services Administration:			
-- Health Resources and Services	$26,693	$24,407	$15,844
-- Health Professions Graduate Student Loan	15,714	36,588	24,673
-- Health Education Loans	27,329	27,179	26,969
-- Nurse Training Fund	6,636	6,251	5,923
-- Medical Facilities Guarantee and Loan Fund	35,843	28,687	29,195
-- Vaccine Injury Compensation Trust Fund	66,395	66,395	66,395
Centers for Disease Control	4,537	--	--
National Institutes of Health	63,634	--	--
Alcohol, Drug Abuse, and Mental Health Admin:			
-- Alcohol, Drug Abuse, and Mental Health	503	--	--
-- Construction and Renovation for St. Elizabeth's Hospital	1,281	--	--
Office of the Assistant Secretary for Health	50	--	--
Subtotal, PHS (Labor/HHS)	248,615	189,507	168,999
Indian Health Service	68,641	1,270	1,270
Total, PHS	$317,256	$190,777	$170,269

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUMMARY

ANALYSIS OF UNOBLIGATED CARRYOVER BALANCES

Fiscal Years 1989, 1990 and 1991
(Dollars in thousands)

Appropriation	Balance end of FY 1989	Balance end of FY 1990	Balance end of FY 1991
SOCIAL SECURITY ADMINISTRATION			
Federal Old-Age and Survivors Insurance TF	$130,793,872	$188,401,785	$261,638,230
Federal Disability Insurance Trust Fund	6,270,402	9,924,684	15,750,742
Supplemental Security Income	265,840	66,446	66,446
FAMILY SUPPORT ADMINISTRATION			
Family Support Payments	69,937	55,963	55,963
Refugee and Entrant Assistance	3,527	3,527	3,527
OFFICE OF HUMAN DEVELOPMENT SERVICES	1,264	1,264	1,264
Subtotal, HHS (Labor/HHS)	137,653,457	198,643,176	277,685,171
TOTAL, HHS	$137,722,098	$198,644,446	$277,686,441

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Alcohol, Drug Abuse, and Mental Health Administration

1991 Legislative Programs
(Dollars in thousands)

Appropriation/Program	1991 Amount Authorized	1991 Outlays
1. General Mental Health:		
a. Research:		
General - Section 301 of the Public Health Service Act (PHSA)	Indefinite	$140,782
Instrumentation Grants - PHSA Section 501	$5,000	250
Research Training - PHSA Section 487	Indefinite	6,450
Research Management & Support - PHSA Section 301	Indefinite	40,068
b. Demonstrations:		
Community Support - PHSA Section 301	Indefinite	6,179
Homeless Demonstrations - P.L. 100-628, Section 621	Indefinite	1,381
c. Protection and Advocacy - P.L. 100-509	Indefinite	1,600
d. Clinical Training - PHSA Section 303	Indefinite	3,900
2. Drug Abuse:		
a. Research:		
General Research - PHSA Section 301 and 517	Indefinite	53,672
Instrumentation Grants - PHSA Section 501	$5,000	101
Research Training - PHSA Section 487	Indefinite	990
Research Management & Support - PHSA Section 301	Indefinite	30,671
b. Demonstrations - PHSA Section 509G	Indefinite	16,490
3. Alcohol:		
a. Research:		
General Research - PHSA Sections 301 and 513(a)	Indefinite	39,729
Instrumentation Grants - PHSA Section 501	$5,000	96
Research Training - PHSA Section 487	Indefinite	677
Research Management & Support - PHSA Section 301	Indefinite	10,995
b. Demonstrations:		
PHSA Section 301 and 513(b)	Indefinite	$4,939

4. Substance Abuse Prevention:		
a. Demonstrations --		
PHSA Sections 508.....	Indefinite	$29,939
P.L. 100-690, Section 3521.....	$60,000	3,099
b. Clinical Training -		
PHSA Section 508.....	Indefinite	4,034
c. Program Management & Support -		
PHSA Section 508.....	Indefinite	2,212
5. Treatment:		
a. Treatment Improvement Programs -		
PHSA Sections 301, 311, 509C, and 516.....	---	31,798
b. Grants to States:		
ADMS Block Grant -		
PHSA Title XIX, Section 1911(a)...	Indefinite	555,893
Homeless -		
PHSA Section 535.....	Indefinite	13,481
6. Buildings and Facilities:		
PHSA Section 301.....	Indefinite	2,219
7. Office of the Administrator:		
PHSA Section 301.....	Indefinite	11,150
Total Outlays.....		$1,012,795

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

PUBLIC HEALTH SERVICE

ASSISTANT SECRETARY FOR HEALTH

1991 Legislative Programs

(Dollars in thousands)

Office of the Assistant Secretary for Health

Extension of Expired Legislation:	Budget Authority	Outlays
1. Adolescent Family Life.....	$9,431	$9,794
2. Family Planning.....	139,135	59,820
New Legislation		
PHS Commissioned Corp Retirement Fund	245,729	96,729

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

HEALTH CARE FINANCING ADMINISTRATION

1991 Legislative Program
(Dollars In Thousands)

Appropriation/Program	Budget Authority	Outlays
Survey and Certification Revolving Fund		
Proposed for Later Transmittal:		
Consolidation of the Health Facility Inspection Programs From the Medicare Survey Activities, Medicaid Survey Activities, and and a New Program of Clinical Laboratory Inspections Under the Clinical Laboratory Improvement Amendments of 1988.	N/A	N/A
Program Management		
Financing of the Medicare Survey and Certification Activity Under the Survey and Certification Revolving Fund	-175,815	-175,815
Financing of Survey and Certification Administrative Costs Under the Survey and Certification Revolving Fund	-38,104	-38,104

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

HEALTH CARE FINANCING ADMINISTRATION

1991 Legislative Program
(Dollars In Thousands)

Appropriation/Program		Budget Authority	Outlays
Grants to States for Medicaid			
Proposed for Later Transmittal:			
1.	Managed Care Initiative	25,000	25,000
2.	Implementation of the Survey and Certification Revolving Fund including the Medicaid Survey and Certification Activities	-113,457	-113,457

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

HEALTH CARE FINANCING ADMINISTRATION

1991 Legislative Program
(Dollars In Thousands)

Appropriation/Program		Budget Authority	Outlays
Federal Hospital Insurance (HI)			
Proposed for Later Transmittal:			
1.	Retain Hospital Capital Payment Reduction of 25% Urban and 15% Rural.	N/A	-1,530,000
2.	Require All State and Local Employees Hired Before March 31, 1986, to Pay the Medicare Hospital Insurance Tax.	1,866,000	N/A
3.	Reduce the Factor for Indirect Medical Education to 4.05 Percent.	N/A	-1,030,000
4.	Reduce Graduate Medical Education Payments for Classroom and Certain Overhead Costs.	N/A	-170,000
5.	Set the PPS Market Update at Marketbasket Minus 1.5 Percent for all Hospitals	N/A	-640,000
6.	Cap Intern and Resident to Bed Ratios at FY 1989 Levels	N/A	-10,000
7.	Prospective Payment for SNFs	N/A	-70,000
8.	Pay HMO's at 100% of the AAPCC	N/A	100,000

DEPARTMENT OF HEALTH AND HUMAN SERVICES

HEALTH CARE FINANCING ADMINISTRATION

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1991 Legislative Program
(Dollars In Thousands)

Appropriation/Program		Budget Authority	Outlays
Supplementary Medical Insurance			
Proposed for Later Transmittal:			
1.	Reduce prevailing charge levels for procedures identified by OBRA 89 as overpriced.	N/A	-110,000
2.	Increase customary and prevailing charge levels for primary care services only.	N/A	-450,000
3.	Reduce payments by up to 25% in overpriced localities.	N/A	-50,000
4.	Limit payments for technical components of diagnostic and radiological tests to the national median.	N/A	-60,000
5.	Increase customary charges for new physicians.	N/A	-50,000
6.	Eliminate duplicate payments to hospitals for physicians' assistants services.	N/A	-5,000
7.	Reduce radiology fee schedule professional component conversion factors.	N/A	-110,000
8.	Reduce anesthesiology fee schedule professional N/A component conversion factors.	N/A	-50,000

DEPARTMENT OF HEALTH AND HUMAN SERVICES

HEALTH CARE FINANCING ADMINISTRATION

1991 Legislative Program
(Dollars In Thousands)

Appropriation/Program		Budget Authority	Outlays
Supplementary Medical Insurance			
Proposed for Later Transmittal:			
9.	Limit payments for anesthesia to a single fee.	N/A	-70,000
10.	Eliminate payments for assistants-at-surgery.	N/A	-120,000
11.	Reduce surgical global fees.	N/A	-50,000
12.	Reduce payment for capital for hospital outpatient departments.	N/A	-100,000
13.	Reduce payments for certain outpatient hospital services by 10%.	N/A	-570,000
14.	Pay for enteral and parenteral nutrients, supplies, equipment by fee schedules.	N/A	-10,000
15.	Establish a national cap on Medicare DME fee schedules; limit updates on carrier fee schedules.	N/A	-130,000
16.	Reduce oxygen payments by five percent.	N/A	-20,000
17.	Change the basis for the fee schedule for certain items of DME; limit the duration of monthly rental payments.	N/A	-90,000
18.	Permit Medicare carriers to require prior authorization when the carrier has evidence of overutilization of part B services.	N/A	-64,000

DEPARTMENT OF HEALTH AND HUMAN SERVICES

HEALTH CARE FINANCING ADMINISTRATION

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1991 Legislative Program
(Dollars In Thousands)

Appropriation/Program		Budget Authority	Outlays
Supplementary Medical Insurance			
Proposed for Later Transmittal:			
19.	Extend Medicare secondary payor for ESRD from 12 months to 18 months.	N/A	-30,000
20.	Lower limits on carrier fee schedules for clinical laboratory tests.	N/A	-50,000
21.	Limit fee updates for clinical labs	N/A	-10,000
22.	Reduce fee schedule to match physician discounting.	N/A	1/
23.	Reform payments to teaching hospitals for graduate medical education.	N/A	-35,000
24.	Pay HMO's at 100% of the AAPCC	80,000	80,000

1/ Estimate currently being developed.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

SOCIAL SECURITY ADMINISTRATION

Legislative Proposals

	($ in millions) Budget Authority	Outlays
Disability Insurance		
1. Cover all newly hired District of Columbia government employees . . .	Negl.	- -
2. Cover State and local government employees not covered under a State or local retirement system	+$219	- -
3. Modify pre-effectuation review requirement for applicants for disability benefits	- -	-$2
4. Revise the advance tax transfer provision so that the trust fund will be credited with Social Security taxes on an as-received basis throughout the month	-$64	-$64
5. Fill coverage gaps in the railroad pension system by paying title II benefits to those not covered . . .	-$1	+$5
6. Recover overpayments to former beneficiaries through use of an income tax refund offset	- -	-$20
7. Interest impact of coverage extensions	+$4	- -
Total, legislative proposals . . .	+$158	-$81

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

SOCIAL SECURITY ADMINISTRATION

Legislative Proposals

	($ in millions) Budget Authority	Outlays
Old-Age and Survivors Insurance		
1. Cover all newly hired District of Columbia government employees . . .	+$2	- -
2. Cover State and local government employees not covered under a State or local retirement system	+$2,044	+$4
3. Change the payroll tax deposit schedule for large employers . . .	+$450	- -
4. Revise the advance tax transfer provision so that the trust fund will be credited with Social Security taxes on an as-received basis throughout the month	-$561	-$597
5. Fill coverage gaps in the railroad pension system by paying title II benefits to those not covered . . .	-$3	+$57
6. Recover overpayments to former beneficiaries through use of an income tax refund offset	- -	-$59
7. Modify dependency requirements for children adopted by a surviving spouse	- -	Negl.
8. Interest impact of coverage extensions	+$45	- -
Total, legislative proposals . . .	+$1,977	-$595

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

SOCIAL SECURITY ADMINISTRATION

Legislative Proposals

	($ in millions)	
	Budget Authority	Outlays
Supplemental Security Income		
1. Charge a fee from States which have Federally-administered State supplements (phase-in to occur over a 3-year period)	-$55	-$55

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Family Support Administration

1991 Legislative Programs
(Dollars in thousands)

Appropriation/Program	Budget Authority	Outlays
75-1501-0-1-609		
FAMILY SUPPORT PAYMENTS		
-- CSE Cost Recovery	-$30,000	-$30,000
-- AFDC Prospective Withholding	-22,400	-22,400
-- CSE Program Efficiency	-10,000	-10,000
-- CSE Expansions	30,000	30,000
TOTAL	-$32,400	-$32,400

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of Human Development Services
(Name of OPDIV)

1991 Legislative Programs
(Dollars in thousands)

Appropriation/Program	Budget Authority	Outlays
Human Development Services Extension Legislative		
Head Start	$1,886,315	$1,620,842
Child Development Associate Scholarships	1,431	1,421
Dependent Care Planning and Development	13,178	13,017
Developmental Disabilities State Grants	61,939	61,452
Protection and Advocacy	20,484	20,320
Projects of National Significance	2,862	2,843
University Affiliated Programs	13,192	13,065
New Legislative Proposal		
Child Welfare Services	47,352	37,882
Total, Human Development Services	$2,046,753	$1,548,485
Payments to States for Foster Care and Adoption Assistance		
Current Law	$2,679,544	$2,488,525
Savings associated with legislative proposal	-160,909	-120,682
Transfer to "Human Development Services"	-47,352	-37,882
Total, Payments to States for Foster Care and Adoption Assistance	$2,471,283	$2,329,961

HEALTH RESOURCES AND SERVICES
Language Analysis

Language Provision	Explanation
Of which $25,000,000 of funds available under Title V of the Social Security Act shall be available, notwithstanding the provisions of Title V of that Act, for grants for One-Stop Shopping;	The langauge for the "One-stop Shopping" initiative would exempt these funds from the Block Grant (85 percent/ SPRANS 15 percent) distribution required by Title V (as amended) and suppport a special grant initiative targeted at improving the delivery of health care services for pregnant women and infants.
Provided, that notwithstanding Section 838 if the public Health Service Act, not exceed $15,000,000 of funds returned to the Secretary pursuant to section 839(c) of the Public Health Service Act or pursuant to a loan agreement under section 740 or 835 of the Act shall first be applied to meet the obligations of the fund established by section 734 of the Act.	HRSA proposes to use funds collected from the Health Professions and Nursing Student loan revolving funds and transfer to the Student Loan Insurance Fund of the Health Education Assistance Loan Program, without respect to funding Ad Hoc hospitals.
Provided, further that of the total amount appropriated $107,000,000 shall be for Minority Health Improvement Initiative, and shall become available when authorized by law.	This langauge allows the Health Resources and Services Administration to address the disparities in the health status of minorities and their underepresentation in the health professions. Specifically the funds are intended to strengthen the the national capacity to train minority students as well a provide a great deal of care to minority population.

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Provided further, That amounts available from Public Health Service unobligated balances shall be available to meet the obligations of the fund established by section 734 of the Act.

This language allows HRSA to transfer PHS unobligated balances to meet obligations to the Student Loan Insurance Fund.

Provided further, That in addition to fees authorized by section 427(b) of the Health Care Quality Improvement Act of 1986, fees shall be collected for the disclosure of information under the Act sufficient to recover the full costs of operating the National Care Quality Improvement Databank, and shall remain available until expended to carry out the Health Care Quality Improvement Act.

The language provides for the databank to be completely self-financed thru the creation of user fees and would be available until expended.

Preventive Health Services

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Language Analysis

Language Provision	Explanation
"...including insurance of official motor vehicles in foreign countries....."	No specific authorization exists for the provision regarding insurance; however, experience of the Centers for Disease Control in stationing Public Health Service officials overseas and at the Mexican Border indicates that this provision is essential. Unless adequate automobile insurance is provided, Public Health Service officials could be subject to arbitrary arrest if they were involved in an accident.
"...and hire, maintenance, and operation of aircraft....."	The Centers for Disease Control must maintain the ability to hire aircraft for testing of new insecticides and formulations and for applying the insecticides when outbreaks of mosquito-borne disease, such as encephalitis, occur in populous areas where no other method can be used to control the spread of the disease.
"...of which $7,900,000 shall remain available until expended and shall be for construction and renovation of facilities....."	Repair and construction projects, require lead time for planning, designing, and contracting procedures, which require longer than the fiscal year to complete and obligate funds.
"...That training of [private persons] shall be made subject to reimbursement or advances to this appropriation for not in excess of the full cost of such training..."	Provides specific authorization for depositing funds to this appropriation which are collected for training up to the cost of the training provided.

Language Provision	Explanation
"...that funds appropriated under this heading shall be available for payment of the costs of medical care, related expenses, and burial expenses hereafter incurred by or on behalf of any person who had participated in the study of untreated syphilis initiated in Tuskegee, Alabama, in 1932, in such amounts and subject to such terms and conditions as prescribed by the Secretary of Health and Human Services and for payment, in such amounts and subject to such terms and conditions, of such costs and expenses hereafter incurred by or on behalf of such person's wife or offspring determined by the Secretary to have suffered injury or disease from syphilis contracted from such person..."	Provides specific authorization for payment of cost of medical care, related expenses, and burial expenses for participants in the study of untreated syphilis. It also provides for payment of cost and expenses incurred by or on behalf of the participant's spouse or offspring who have suffered injury or disease from syphilis contracted from such participants.
"...that collections from user fees may be credited to this appropriation....."	Provides specific authorization to allow all funds collected as user fees to be deposited to this appropriation.
"...that amounts received by the National Center for Health Statistics from reimbursable and interagency agreements and the sale of data tapes may be credited to this appropriation and shall remain available until expended:....."	Provides specific authorization to allow all funds collected by the National Center for Health Statistics from reimbursable and interagency agreements to be deposited to this appropriation and to remain available until expended.

Language Provision	Explanation
"...that in addition to amounts provided herein, up to $19,000,000 shall be available from amounts available under section 213 of the Public Health Service Act, to carry out the National Center for Health Statistics surveys....."	Provides specific authorization for use of evaluation funds by the National Center for Health Statistics to help finance health surveys.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

HEALTH CARE FINANCING ADMINISTRATION

Identification of Appropriations Language Provisions, Earmarks, etc., Which Modify or Go Beyond Authorizing Legislation

PROGRAM MANAGMENT

Provided, That $100,000,000 of appropriated trust funds shall be expended only to the extent necessary to meet unanticipated workloads of agencies or organizations with which agreements have been made to participate in the administration of title XVIII and after maximum absorption of such costs within the remainder of the existing limitation has been achieved. . .	Reserves $100,000,000 of the appropriated Trust Fund transfer as a contingency fund, to be utilized by the Medicare Contractors budget activity in the event that workloads exceed current projections.
Provided further, That $73,000,000 of said trust funds shall be expended only to the extent necessary to carry out provisions of Public Law 101-239. . .	Reserves $73,000,000 of the appropriated Trust Fund transfer as a contingency fund to be utilized only to carry out provisions of the Omnibus Budget Reconciliation Act of 1989, as necessary, including Contractor Transition costs.
Provided further, That this appropriation shall be the exclusive appropriation for administrative and evaluation costs of research and demonstration projects authorized by section 402 of the Social Security Amendments of 1967, as amended. . .	This new provision limits the funding for research projects operated under Section 402 to this appropriation, thereby prohibiting the funding of such projects through direct apportionments of Medicare Trust Funds.
Provided further, That none of the funds appropriated here shall be obligated for any survey, inspection, or certification activities authorized by Titles XVIII or XIX of the Social Security Act or section 353 of the Public Health Service Act. . .	This new provision removes obligational authority for all Medicare and Medicaid survey and certification activities from the Program Management account, relegating all such authority to the new Survey and Certification Revolving Fund account.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

HEALTH CARE FINANCING ADMINISTRATION

Identification of Appropriations Language Provisions, Earmarks, etc., Which Modify or Go Beyond Authorizing Legislation

GRANTS TO STATES TO MEDICAID

Provided further, that no funds shall be obligated from this account for survey and certification activities authorized by Title XIX of the Social Security Act.	The new language removes funding for Medicaid survey and certification activities ($113.5 million) because all survey and certification activities will be financed through the Survey and Certification Revolving Fund Account.
Payment under Title XIX may be made for any quarter with respect to a State plan amendment in effect during such quarter, if submitted in or prior to such quarter and approved in that or any subsequent quarter.	This section makes clear that funds are available with respect to State plans or plan amendments only for expenditures on or after the beginning of the quarter in which a plan or amendment is submitted to HHS for approval.

T-11

DEPARTMENT OF HEALTH AND HUMAN SERVICES

HEALTH CARE FINANCING ADMINISTRATION

Identification of Appropriations Language Provisions, Earmarks, etc., Which Modify or Go Beyond Authorizing Legislation

SURVEY AND CERTIFICATION REVOLVING FUND

There is hereby established in the Treasury of the United States a Revolving Fund. Amounts in the Fund shall be available to the Secretary, without fiscal year limitation, to finance the costs of carrying out Federal and State survey and certification activities under Titles XVIII and XIX of the Social Security Act and activities under section 353 of the Public Health Service Act (42 U.S.C. 263a). Fees authorized by this paragraph and section 353(m) of the Public Health Service Act shall be deposited in and credited to the Fund.	Authorizing language which establishes a revolving fund to finance the inspection programs authorized under the Social Security Act and the Public Health Service Act. This provision also allows for obligations and expenditures to be made and carried from one fiscal year to the next.
Notwithstanding any other provision of law, including but not limited to sections 1903 and 1919(g) of the Social Security Act, the Secretary shall establish and collect annually user fees from all providers and suppliers of services or items requesting certification under Titles XVIII or XIX of the Social Security Act (except clinical laboratories otherwise inspected and certified under section 353 of the Public Health Service Act) and payment thereof shall be made a condition of participation under said Titles.	This provision authorizes the assessment of fees and requires that the payment of the fees be mandatory for facilities requesting program participation.

T-11

DEPARTMENT OF HEALTH AND HUMAN SERVICES

HEALTH CARE FINANCING ADMINISTRATION

Identification of Appropriations Language Provisions, Earmarks, etc., Which Modify or Go Beyond Authorizing Legislation

SURVEY AND CERTIFICATION REVOLVING FUND

Such fees shall be determined annually in an amount sufficient to cover the estimated full cost of survey and certification activities not otherwise covered by fees collected pursuant to section 353(m) of the Public Health Service Act.	This provides that the fees assessed shall fund all activities related to the surveys and certification, i.e., administrative costs as well as direct survey costs.
These fees shall be collected annually from each provider or supplier, regardless whether the provider or supplier will be surveyed in the year for which fees are being charged, and fees may be collected through deductions from payments to be made under Titles XVIII and XIX of the Social Security Act.	This provision allows for the fees to be collected in advance of the actual surveys and certifications, even in a year in which no surveys are conducted. It also provides that the fees may be deducted from payments for services or supplies normally made under the Medicare and Medicaid programs.
Fees may vary by group or classification of provider or supplier, or by the relative complexity, type, or estimated cost of planned surveys, based on such considerations as the Secretary deems appropriate.	This allows the Secretary to exercise discretion in developing the amount of the fees to be assessed.
Fees established under this paragraph and section 353(m) of the Public Health Service Act shall be set and collected to maintain a minimum balance in the Fund equal to one month's estimated expenses.	This provides for a minimum balance to be maintained at all times.

T-11

DEPARTMENT OF HEALTH AND HUMAN SERVICES

HEALTH CARE FINANCING ADMINISTRATION

Identification of Appropriations Language Provisions, Earmarks, etc., Which Modify or Go Beyond Legislation

PAYMENTS TO THE HEALTH CARE TRUST FUNDS

The Committee has not included bill language proposed by the Administration indicating that the HI and SMI Trust Funds should not be used to support catastrophic coverage costs. This language would merely reinforce what is already clear in authorizing statute.

HCFA advanced this language in an effort to maintain the integrity of the self-financing aspects of the catastrophic health insurance program. However, the Medicare Catastrophic Coverage Repeal Act of 1989 (P.L. 101-234) eliminated the HI and SMI catastrophic health insurance programs and the need for this language.

T-11

DEPARTMENT OF HEALTH AND HUMAN SERVICES

SOCIAL SECURITY ADMINISTRATION

Identification of Appropriation Language Provisions, Earmarks, etc.
Which Modify or Go Beyond Authorizing Legislation

Language Provision in the Limitation on Administrative Expenses (LAE) Account	Explanation
"*Provided*, That travel expense payments under section 1631(h) of such Act for travel to hearings may be made only when travel of more than seventy-five miles is required:"	Authorizing legislation enacted in the Social Security Disability Amendments of 1980 specifies that the Secretary "shall pay" for travel incident to medical examinations and for claimants, their representatives, and witnesses to attend reconsideration interviews and hearings for title XVI claims. This provision restores the mileage limitation which was established in regulations before enactment of the 1980 Disability Amendments and makes travel reimbursement policy the same for SSI and Social Security claimants.

Language Provision in the Special Benefits for Disabled Coal Miners Account	Explanation
"...including the payment of travel expenses on an actual cost or commuted basis, to an individual, for travel incident to medical examinations, and when travel of more than 75 miles is required, to parties, their representatives, and all reasonably necessary witnesses for travel within the United States, Puerto Rico, and the Virgin Islands, to reconsideration interviews and to proceedings before administrative law judges..."	Authorizing legislation did not specify whether or not travel incident to medical examinations or travel for claimants, their representatives, and witnesses to attend reconsideration interviews and hearings was a necessary administrative expense. This provision, which permits the payment of these travel expenses for occasions requiring travel of more than 75 miles, reduces financial hardship to claimants. Similar language for the Social Security trust fund programs and SSI is present in subsections 201(j), 1631(h) and 1817(i) of the Social Security Act.
"...*Provided*, That monthly benefit payments shall be paid consistent with section 215 (g) of the Social Security Act."	This language provides the authority needed to compute black lung benefit payments on the same basis as Social Security and SSI benefits.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Family Support Administration
Office of Refugee Resettlement

Identification of Appropriation Language Provisions, Earmarks, etc.,
Which Modify or Go Beyond Authorizing Legislation

Language Provision	Explanation
"For making payments for refugee and entrant assistance activities pursuant to title IV of the Immigration and Nationality Act..."	The 1991 budget request is based on authority of the Refugee Act of 1980 (P.L. 96-212) enacted on March 17, 1980 and the Refugee Assistance Extension Act of 1986 (P.L. 99-605), which amend title IV of the Immigration and Nationality Act. The legislation repeals the Indochina Migration and Refugee Assistance Act of 1975, and eliminates the domestic assistance provisions of the Migration and Refugee Assistance Act of 1962. These two Acts were the previous authorities for operating the Refugee Assistance programs. Public Law 96-212 authorizes services to eligible refugees.
"... and section 501 of the Refugee Education Assistance Act of 1980 (Public Law 96-422,...".)	The 1991 budget request is also based on authority of the Refugee Education Assistance Act of 1980 (P.L.-422), which authorizes refugee assistance services to Cuban and Haitan entrants.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Family Support Administration
Office of Community Services

Identification of Appropriation Language Provisions, Earmarks, etc.,
Which Modify or Go Beyond Authorizing Legislation

Language Provision	Explanation
"For making payments under the Stewart B. McKinney Homeless Act..."	This language provides funds under the Emergency Community Services Homeless Grant Program to assist families and individuals who are homeless or about to become homeless. This program is authorized under Subtitle D of the Stewart B McKinney Homeless Assistance Act (P.L. 100-77) as amended.

T-11

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of Human Development Services
(Name of OPDIV)

Identification of Appropriation Language Provisions, Earmarks, etc., Which Modify or Go Beyond Authorizing Legislation

Language Provision	Explanation
Social Services Block Grant	
...monthly payments to States for..	Language is added to stipulate that payments will be made to States in twelve monthly allotments.
Human Development Services	None.
Payments to States for Foster Care and Adoption Assistance	
...Provided, That notwithstanding section 474(a) of said Act, no payments shall be made to any State from amounts made available under this Act, for expenditures for administration of the State plan for Foster Care under section 472 of such Act for fiscal year 1991 in excess of an amount equal to 110 percent of the total payments made such State for such expenditures for fiscal year 1990 (as determined on the basis of claims submitted by the State and received by the Secretary on or before May 15, 1991, and determined allowable by the Secretary by September 30, 1991:)	Language is added to limit the growth of administrative costs to 10 percent.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUMMARY

Total Budget Authority by Fund

Fiscal Years 1971 through 1991
(Dollars in thousands)

Fiscal Year	General Funds	Trust Funds	Total
1971	$10,499,428	$38,892,424	$49,391,852
1972	14,956,853	43,207,460	58,164,313
1973	16,288,211	49,585,266	65,873,477
1974	16,789,968	57,703,306	74,493,274
1975	19,548,833	66,676,153	86,224,986
1976	23,134,813	70,682,325	93,817,138
1977	23,911,478	81,169,295	105,080,773
1978	42,768,718	89,594,736	132,363,454
1979	45,885,170	102,088,941	147,974,111
1980	54,901,436	117,439,214	172,340,650
1981	61,218,233	132,949,654	194,167,887
1982	64,011,264	146,207,455	210,218,719
1983	69,348,795	184,510,643	253,859,438
1984	75,576,393	180,582,158	256,158,551
1985	83,439,129	198,160,418	281,599,547
1986	83,541,512	205,772,923	289,314,435
1987	90,014,820	227,606,534	317,621,354
1988	101,536,486	259,056,279	360,592,765
1989	113,353,706	286,071,956	399,425,662
1990	125,666,435	311,414,009	437,080,444
1991	$134,245,279	$345,334,390	$479,579,669

DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUMMARY
AUTHORIZATIONS VS. APPROPRIATIONS

Fiscal Years 1981 through 1991
(Dollars in thousands)

	1981		1982		1983		1984	
	DEFINITE AUTH.	APPRO/ DEF. AUTH.	DEFINITE AUTH.	APPRO/ DEF. AUTH.	DEFINITE AUTH.	APPRO/ DEF. AUTH.	DEFINITE AUTH.	APPRO/ DEF. AUTH.
PUBLIC HEALTH SERVICE								
Health Resources and Services Administration	$1,734,426	$1,517,653	$2,113,300	$1,530,842	$1,979,550	$1,345,841	$1,118,800	$1,121,122
Centers for Disease Control	431,000	120,382	169,500	63,236	88,500	72,428	95,500	80,992
National Institutes of Health:								
-- National Library of Medicine	18,500	9,831	7,500	7,500	--	7,500	--	7,500
-- National Cancer Institute	1,128,600	--	1,232,200	--	--	962,581	--	1,081,581
-- National Heart, Lung & Blood Inst.	613,600	--	616,100	--	595,736	--	--	704,939
-- National Institute of Child Health and Human Development	138,900	--	--	--	--	--	--	--
Alcohol, Drug Abuse, and Mental Health Administration	753,500	414,797	774,500	513,767	707,500	485,337	651,287	576,943
Office of the Assistant Secretary for Health	322,500	162,631	93,000	54,507	100,760	60,052	128,000	69,648
HEALTH CARE FINANCING ADMINISTRATION	4,000	1,718	4,000	1,718	4,000	1,718	4,000	1,718
FAMILY SUPPORT ADMINISTRATION								
Payments to States for Family Support Activities	--	--	--	--	--	--	--	--
LIHEAP	--	--	1,875,000	1,875,000	1,875,000	1,975,000	1,875,000	2,075,000
ORR	200,000	144,492	200,000	153,148	200,000	106,062	114,000	76,100
SLIAG	--	--	--	--	--	--	--	--
WIN	--	365,000	--	280,760	--	270,760	--	270,760
OCS	--	--	389,375	366,075	389,375	385,500	389,375	352,300
OFFICE OF HUMAN DEVLEOPMENT SERVICES								
Social Services Block Grant	2,916,000	2,916,000	2,400,000	2,400,000	2,675,000	2,675,000	2,700,000	2,675,000
Human Development Services	$1,457,000	$885,659	$291,000	$231,000	2,261,694	2,109,973	2,080,136	1,925,913
Foster Care/Adoption Assistance	--	--	--	--	$266,000	$156,326	$266,000	$165,000

DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUMMARY
AUTHORIZATIONS VS. APPROPRIATIONS

Fiscal Years 1981 through 1991
(Dollars in thousands)

	1985		1986		1987		1988	
	DEFINITE AUTH.	APPRO/ DEF. AUTH.	DEFINITE AUTH.	APPRO/ DEF. AUTH.	DEFINITE AUTH.	APPRO/ DEF. AUTH.	DEFINITE AUTH.	APPRO/ DEF. AUTH.
PUBLIC HEALTH SERVICE								
Health Resources and Services Administration	$660,400	$526,800	$702,200	$508,051	$1,231,650	$1,002,075	$1,221,200	$957,300
Centers for Disease Control	225,500	181,910	242,000	184,828	276,500	220,500	150,000	98,134
National Institutes of Health:								
-- National Library of Medicine	--	7,790	12,000	7,790	13,000	(9,410)	14,000	9,414
-- National Cancer Institute	--	--	1,262,000	1,146,763	1,344,000	1,339,658	1,424,000	1,379,383
-- National Heart, Lung & Blood Inst.	--	--	891,000	820,762	961,000	913,136	1,025,000	926,030
-- National Institute of Child Health and Human Development	--	--	--	--	--	--	--	--
Alcohol, Drug Abuse, and Mental Health Administration	656,000	624,600	701,000	632,234	1,435,500	768,855	1,203,713	723,889
Office of the Assistant Secretary for Health	136,500	72,057	101,750	55,780	129,750	66,302	182,779	169,403
HEALTH CARE FINANCING ADMINISTRATION	4,000	1,718	4,000	1,200	4,000	2,150	4,000	2,200
FAMILY SUPPORT ADMINISTRATION								
Payments to States for Family Support Activities	--	--	--	--	--	--	--	--
LIHEAP	2,140,000	2,100,000	2,275,000	2,099,100	2,050,000	1,825,000	2,132,000	1,531,000
ORR	--	--	--	--	83,544	76,627	87,049	51,629
SLIAG	--	--	--	--	--	--	1,000,000	930,000
WIN	--	266,760	--	212,344	--	126,000	--	92,551
OCS	400,000	372,435	415,000	352,166	390,000	368,736	417,500	382,290
OFFICE OF HUMAN DEVLEOPMENT SERVICES								
Social Services Block Grant	2,725,000	2,725,000	2,700,000	2,583,000	2,700,000	2,700,000	2,750,000	2,700,000
Human Development Services	2,129,180	1,877,769	2,669,500	1,820,749	2,279,589	2,025,816	2,689,755	2,312,453
Foster Care/Adoption Assistance	$266,000	$200,000	$266,000	$198,099	$311,000	$284,250	$45,000	$45,000

DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUMMARY
AUTHORIZATIONS VS. APPROPRIATIONS

Fiscal Years 1981 through 1991
(Dollars in thousands)

	1989		1990		1991	
	DEFINITE AUTH.	APPRO/ DEF. AUTH.	DEFINITE AUTH.	APPRO/ DEF. AUTH.	DEFINITE AUTH.	APPRO/ DEF. AUTH.
PUBLIC HEALTH SERVICE						
Health Resources and Services Administration	$1,466,600	$1,301,011	$1,377,920	$902,685	$1,168,560	$710,399
Centers for Disease Control	263,000	180,789	154,000	35,052	10,000	3,949
National Institutes of Health:						
-- National Library of Medicine	14,000	9,673	--	12,852	--	13,191
-- National Cancer Institute	1,600,000	1,537,188	--	1,627,709	--	1,658,266
-- National Heart, Lung & Blood Inst.	1,201,000	1,046,259	--	1,072,335	--	1,112,502
-- National Institute of Child Health and Human Development	--	--	--	--	--	--
Alcohol, Drug Abuse, and Mental Health Administration	2,353,300	1,176,819	183,500	--		
Office of the Assistant Secretary for Health	162,295	152,295	219,556	192,357	74,000	206,000
HEALTH CARE FINANCING ADMINISTRATION	4,000	2,200	4,000	2,200	4,000	2,200
FAMILY SUPPORT ADMINISTRATION						
Payments to States for Family Support Activities	600,000	1/	800,000	463,038	1,000,000	1,000,000
LIHEAP	1,383,200	1,383,200	1,100,000	1,100,000	1,050,000	1,050,000
ORR	--	--	--	--	--	--
SLIAG	1,000,000	930,000	1,000,000	302,576	1,000,000	302,597
WIN	--	91,440	--	2/	--	2/
OCS	482,000	380,598	390,639	388,780		
OFFICE OF HUMAN DEVLEOPMENT SERVICES						
Social Services Block Grant	2,700,000	2,700,000	2,800,000	2,762,200	2,800,000	2,800,000
Human Development Services	2,781,631	2,389,200	2,943,439	2,554,930	1,466,379	1,090,544
Foster Care/Adoption Assistance	$45,000	$45,000	$50,000	$50,000	$60,000	$60,000

1/ $57,000,000 is included in the Family Support Payments account for administering JOBS activities.
2/ In FY 1990, this program was replaced by the Job Opportunities and Basic Skills (JOBS) training program. Transitional funding for WIN in FY 1990 is provided under the Payments to States for AFDC Work Programs appropriation account.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUMMARY

Appropriations for which Funds Lapsed in FY 1989

(Dollars in thousands)

Appropriation	FY 1989 Lapsed Funds
PUBLIC HEALTH SERVICE	
Health Resources and Services Administration	$1,936
Centers for Disease Control	63
National Institutes of Health	1,852
Alcohol, Drug Abuse, and Mental Health Administration	369
Health Care Policy and Research	91,819
Office of the Assistant Secretary for Health	397
Subtotal, PHS (Labor/HHS)	96,436
Food and Drug Administration	63
Indian Health Service	1,679
Total, PHS	98,178
HEALTH CARE FINANCING ADMINISTRATION	2,943
SOCIAL SECURITY ADMINISTRATION	10,776
FAMILY SUPPORT ADMINISTRATION	17,214
OFFICE OF HUMAN DEVELOPMENT SERVICES	23,138
OFFICE OF THE SECRETARY	1,494
Total, HHS (Labor/HHS)	152,001
OFFICE OF CONSUMER AFFAIRS	10
TOTAL, HHS	$153,753

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUMMARY

Travel by Appropriations, FY 1989-1991
(Dollars in thousands)

Appropriation	FY 1989	FY 1990	FY 1991
PUBLIC HEALTH SERVICE			
Health Resources and Services Administration	$4,335	$4,552	$4,426
Centers for Disease Control	11,305	11,327	12,195
National Institutes of Health	16,694	18,458	19,126
Alcohol, Drug Abuse, and Mental Health Administration	2,557	3,039	3,388
Health Care and Policy Research	--	--	206
Office of the Assistant Secretary for Health	1,113	1,212	1,207
Subtotal, PHS (Labor/HHS)	36,004	38,588	40,548
Food and Drug Administration	11,596	13,631	11,302
Indian Health Service	28,297	30,003	31,593
Total, PHS	75,897	82,222	83,443
HEALTH CARE FINANCING ADMINISTRATION	5,546	5,111	5,361
SOCIAL SECURITY ADMINISTRATION	24,079	17,229	24,417
FAMILY SUPPORT ADMINISTRATION	1,740	1,740	1,740
OFFICE OF HUMAN DEVELOPMENT SERVICES	720	927	1,300
OFFICE OF THE SECRETARY	4,990	6,462	6,501
Subtotal, HHS (Labor/HHS)	73,079	70,057	79,867
OFFICE OF CONSUMER AFFAIRS	44	60	60
TOTAL, HHS	$113,016	$113,751	$122,822

DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUMMARY
PROGRAM MANAGEMENT AND PROGRAM SUPPORT COSTS

FY 1988 through FY 1991
(Dollars in thousands)

	OBJECT CLASSIFICATION	1988 ACTUAL	1989 ACTUAL	1990 EST.	1991 EST.
	PERSONNEL COMPENSATION:				
11.1	Full-time permanent	$1,320,569	$1,383,462	$1,557,152	$1,583,320
11.3	Other than full-time permanent	155,972	163,361	181,948	181,305
11.5	Other personnel compensation	56,899	65,823	66,415	65,915
11.8	Special personal services payments	26,703	29,913	29,253	33,562
11.9	Total personnel compensation	1,560,143	1,642,559	1,834,768	1,864,102
12.1	Civilian personnel benefits	277,583	318,826	344,493	439,194
13.0	Benefits for former personnel	78,581	85,123	93,305	160,501
21.0	Travel and transportation of persons	79,824	88,240	95,837	95,921
22.0	Transportation of things	18,350	21,249	22,642	22,034
23.1	Rental payments to GSA	83,799	87,128	98,041	100,607
23.2	Rental payments to others	33,186	30,444	41,850	65,962
23.3	Communications, utilities, and miscellaneous charges	79,625	89,037	94,519	94,854
24.0	Printing and reproduction	53,666	41,886	45,621	46,583
25.0	Other services	6,093,818	6,624,497	7,244,405	7,247,801
26.0	Supplies and materials	255,043	313,476	327,069	330,395
31.0	Equipment	163,817	173,166	165,587	166,659
32.0	Land and structures	48,864	66,582	139,817	19,137
33.0	Investments and loans	3,513	18,393	15,425	6,368
42.0	Insurance claims and indemnities	308,651,625	330,106,661	355,700,043	374,651,195
43.0	Interest and dividends	925,436	1,094,351	931,125	236,656
92.0	Undistributed	3,204,981	3,216,100	3,364,097	3,478,455
93.0	Limitation on Expenses	3,753,673	3,765,920	3,748,075	4,116,974
	Total, HHS	$325,365,527	$347,783,638	$374,306,719	$393,143,398
	End-of-year employment.....	101,408	117,453	117,993	119,606

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Secretary of Health and Human Services

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